

66(03)  
K 59E



INDIAN AGRICULTURAL  
RESEARCH INSTITUTE, NEW DELHI.

I. A. R. I. G.

MGIPC—SI—6 AR/54—7-7-54—10,000.

46097





ENCYCLOPEDIA OF CHEMICAL TECHNOLOGY

*VOLUME 13*



# **ENCYCLOPEDIA OF CHEMICAL TECHNOLOGY**

*Edited by*      **RAYMOND E. KIRK**  
*Head, Department of Chemistry, Polytechnic Institute of Brooklyn*  
*and*              **DONALD F. OTHMER**  
*Head, Department of Chemical Engineering, Polytechnic Institute of  
Brooklyn*

46097



IARI

*Assistant Editors*  
**JANET D. SCOTT and ANTHONY STANDEN**

**VOLUME 13**

**STILBITE**  
*to*  
**THERMOCHEMISTRY**

**REFERENCE**

46097  
511

**THE INTERSCIENCE ENCYCLOPEDIA, INC. • NEW YORK**

COPYRIGHT 1954, BY  
THE INTERSCIENCE ENCYCLOPEDIA, INC.

---

ALL RIGHTS RESERVED

---

THIS BOOK OR ANY PART THEREOF MUST  
NOT BE REPRODUCED IN ANY FORM WITH-  
OUT PERMISSION OF THE PUBLISHERS IN  
WRITING. THIS APPLIES SPECIFICALLY  
TO PHOTOSTATIC AND MICROFILM  
REPRODUCTIONS.

DISTRIBUTED BY  
INTERSCIENCE PUBLISHERS, INC.  
250 FIFTH AVENUE, NEW YORK 1, N. Y.

PRINTED IN U.S.A. BY  
MACK PRINTING CO., EASTON, PA.

## EDITORIAL STAFF FOR VOLUME 13

Janet D. Scott

Anthony Standen

James A. Lecky

Annette Stern

## CONTRIBUTORS TO VOLUME 13

- J. J. Ayo, Jr.**, General Aniline & Film Corporation, Dycstuff and Chemical Division,  
*Sulfur dyes*
- J. S. Ball**, Bureau of Mines, U.S. Department of the Interior, *Sulfur compounds,*  
*organic*
- C. K. Banks**, Metal and Thermit Corp., *Thermit process*
- R. F. Benenati**, Polytechnic Institute of Brooklyn, *Stoichiometry*
- H. Blanchet**, Freeport Sulphur Company, *Sulfur*
- R. F. Boyer**, The Dow Chemical Company, *Styrene resins and plastics*
- E. E. Campaigne**, Indiana University, *Sulfides, organic*
- H. L. Carolan**, Carbide and Carbon Chemicals Company, A Division of Union Carbide  
and Carbon Corporation, "Dynel and Vinyon" under *Textile fibers (acrylic and*  
*vinyl)*
- B. M. Carter**, General Chemical Division, Allied Chemical & Dye Corporation, *Sul-*  
*furic acid*
- K. A. Clark**, Research Council of Alberta, *Tar sands*
- P. de Mayo**, Birkbeck College, University of London, *Terpenes (sesqui-; tri-)*
- C. H. Demos**, Lederle Laboratories Division, American Cyanamid Company, *Tetra-*  
*cyclines (chlortetracycline)*
- P. H. Dike**, Leeds & Northrup Company, *Temperature measurement*
- E. F. Domino**, University of Michigan, *Stimulants and depressants of the nervous*  
*system*
- John Ehrlich**, Parke, Davis & Company, *Streptomyces antibiotics (chloramphenicol)*
- E. M. Elkin**, Canadian Copper Refiners Limited, *Tellurium and tellurium com-*  
*pounds*
- R. C. Ellingson**, Mead Johnson and Company, "D-Fructose" under *Sugars (com-*  
*mmercial)*
- A. C. Finlay**, Chas. Pfizer & Co., Inc., *Streptomyces antibiotics (carbomycin; viomycin)*
- Lawrence H. Flett**, National Aniline Division, Allied Chemical & Dye Corporation,  
*Succinic acid and succinic anhydride*
- Gregory Flint**, General Chemical Division, Allied Chemical & Dye Corporation, *Sul-*  
*furic acid (sulfur trioxide)*

- E. H. Flynn, The Lilly Research Laboratories, *Streptomyces antibiotics (erythromycin)*  
 Wm. Howlett Gardner, National Aniline Division, Allied Chemical & Dye Corporation, *Succinic acid and succinic anhydride*  
 E. E. Gilbert, General Chemical Division, Allied Chemical & Dye Corporation, *Sulfonation and sulfation*  
 L. B. Gittinger, Jr., Freeport Sulphur Company, *Sulfur*  
 W. C. Goggin, The Dow Chemical Company, *Styrene resins and plastics*  
 J. A. Grant, Owens-Corning Fiberglas Corporation, *Textile fibers (glass)*  
 A. A. Harban, Standard Oil Company (Indiana), *Sulfonic acids*  
 G. C. Harris, Hercules Powder Company, *Terpenes (di-)*  
 J. E. Hawkins, University of Florida, *Terpenes (mono-, acyclic)*  
 Karl M. Herstein, Herstein Laboratories, Inc., *Thallium and thallium compounds*  
 J. L. Hickson, Sugar Research Foundation, Inc., *Sugars (survey); Sugars (commercial)*  
 (in part); *Sugars (derivatives)*  
 F. L. Hilbert, U. S. Process Corp., *Tanning materials (vegetable)*  
 Mary F. Hughes, Refined Syrups & Sugars, Inc., "Invert sugar" under *Sugars*  
 (commercial)  
 M. E. Hultquist, Research Division, American Cyanamid Company, *Sulfa drugs; Sulfonamides*  
 F. L. Jackson, Freeport Sulphur Company, *Sulfur*  
 C. E. Johnson, Standard Oil Company (Indiana), *Sulfonic acids*  
 L. V. Jones, Saran Yarns Co., "Saran" under *Textile fibers (acrylic and vinyl)*  
 George Jura, University of California, *Surface properties*  
 Ernest R. Kaswell, Fabric Research Laboratories, Inc., *Textile testing*  
 Ernest Kuhn, General Aniline & Film Corporation, Dyestuff and Chemical Division, *Sulfur dyes*  
 H. A. Lechevalier, Institute of Microbiology, Rutgers University, *Streptomyces antibiotics (survey; streptomycin; neomycin)*  
 P. M. Levin, E. I. du Pont de Nemours & Co., Inc., Textile Fibers Department, "Acrilon, Orlon, X-51," under *Textile fibers (acrylic and vinyl); Textile fibers (tetrafluoroethylene)*  
 Pat Macaluso, Stauffer Chemical Company, *Sulfur compounds—structures; Sulfur compounds, inorganic*  
 Emma J. McDonald, National Bureau of Standards, U.S. Department of Commerce, *Sugar analysis*  
 J. M. McGuire, The Lilly Research Laboratories, *Streptomyces antibiotics (erythromycin)*  
 J. L. Margrave, University of Wisconsin, *Tellurium and tellurium compounds*  
 George F. Mitchell, General Foods Corporation, *Tea*  
 H. H. Mosher, Arkansas Chemical Company, *Textile technology*  
 L. A. Nelson, Jr., Freeport Sulphur Company, *Sulfur*  
 Mark Nickerson, University of Michigan, *Stimulants and depressants of the nervous system*  
 Richard Pasternack, Chas. Pfizer & Co., Inc., *Tartaric acid*  
 Louise L. Phillips, Refined Syrups & Sugars, Inc., "Invert sugar" under *Sugars*  
 (commercial)  
 O. S. Plantinga, Johnson & Johnson, *Surgical dressings*  
 Louis Preisman, Barium Reduction Corporation, *Strontium compounds*  
 Donald Price, Oakite Products, Inc., *Surface-active agents*  
 L. M. Pruess, Research Division, Lederle Laboratories, American Cyanamid Company, *Tetracyclines (chlortetracycline)*

- Peter P. Regna**, Chas. Pfizer & Co., Inc., *Streptomyces antibiotics (carbomycin; viomycin); Tetracyclines (oxytetracycline; tetracycline)*
- Desmond M. C. Reilly**, Food Machinery and Chemical Corporation (Chemical Divisions), "Strontium hydroxide" under *Strontium compounds*
- E. O. Rhodes**, Koppers Company, Inc., *Tar and pitch*
- E. G. Rietz**, Chicago City Colleges, Wright Branch, *Sulfones; Sulfoxides; Terpenes (mono-, acyclic)*
- W. J. Roberts**, Pennsylvania Industrial Chemical Corporation, *Styrene; Terpene resins*
- W. S. Ropp**, Hercules Powder Company, *Terpenes (mono-, cyclic)*
- S. A. Rossmassler**, E. I. du Pont de Nemours & Co., Inc., Textile Fibers Department, *Textile fibers (polyester)*
- J. S. Ruhoff**, Monsanto Chemical Company, *Sweetening agents*
- L. F. Samler**, Saran Yarns Co., "Saran" under *Textile fibers (acrylic and vinyl)*
- Alvin Schallis**, Stauffer Chemical Company, *Sulfur compounds, inorganic*
- G. B. Shea**, Bureau of Mines, U.S. Department of the Interior, "U.S. deposits" under *Tar sands*
- F. J. Soday**, The Chemstrand Corporation, *Textile fibers, synthetic (survey)*
- H. C. Speel**, Consultant, *Textile technology*
- J. A. Stavrolakis**, Armour Research Foundation, *Thermal analysis*
- R. H. Stevens**, Herty Foundation, *Tall oil*
- A. A. Stonehill**, Ethicon Suture Laboratories, Incorporated, *Surgical sutures*
- James M. Straley**, Tennessee Eastman Company, Division of Eastman Kodak Company, *Sulfuric and sulfurous esters*
- J. A. Struthers**, The Dow Chemical Company, *Styrene resins and plastics*
- R. L. Stubbings**, Lehigh University, *Tanning materials (chemistry; synthetic)*
- Michael Szwarc**, College of Forestry, State University of New York, *Thermochemistry*
- D. F. Taylor**, Fansteel Metallurgical Corporation, *Tantalum and tantalum compounds*
- E. H. Thaete, Jr.**, Freeport Sulphur Company, *Sulfur*
- J. J. Throssel**, College of Forestry, State University of New York, *Thermochemistry*
- Hans Thurnauer**, American Lava Corporation, *Talc*
- Gilberta G. Torrey**, E. I. du Pont de Nemours & Co., Inc., Grasselli Chemicals Department, *Sulfamic acid*
- W. E. Truce**, Purdue University, *Sulfonic acids*
- Selman A. Waksman**, Institute of Microbiology, Rutgers University, *Streptomyces antibiotics (survey; streptomycin; neomycin)*
- A. L. Ward**, Pennsylvania Industrial Chemical Corporation, *Styrene; Terpene resins*
- L. A. Wills**, Consultant, *Sugar manufacture*





## ABBREVIATIONS AND SYMBOLS

A.	Ångström unit(s)	A.S.M.E.	American Society of
A	anion; as, HA		Mechanical Engineers
abs.	absolute	A.S.T.M.	American Society for
a.c.	alternating current		Testing Materials
ac-	alicyclic; as, <i>ac</i> -derivatives of tetrahydronaphthalene	atm.	atmosphere(s), atmospheric
		at. no.	atomic number
A.C.S.	American Chemical Society	at. wt.	atomic weight
addn.	addition	av.	average
A.G.A.	American Gas Association	b. (as, b <sub>11</sub> )	boiling (at 11 mm.)
		B	base; as, B.2HCl
A.I.Ch.E.	American Institute of Chemical Engineers	bbl.	barrel(s)
		Bé.	Baumé
A.I.M.E.	American Institute of Mining and Metallurgical Engineers	b.p.	boiling point
		B.t.u.	British thermal unit(s)
		bu.	bushel(s)
		C.	centigrade
alc.	alcohol, alcoholic	C-	denoting attachment to
alk.	alkaline (not alkali)		carbon; as, <i>C</i> -alkyl
Alk	alkyl		derivatives of aniline
amp.	ampere(s)	cal.	calorie(s)
amp.-hr.	ampere-hour(s)	calcd.	calculated
amt.	amount (noun)	c.f.m.	cubic foot (feet) per
anhyd.	anhydrous		minute
A.P.I.	American Petroleum Institute	cg.	centigram(s)
		c.g.s.	centimeter-gram-second
app.	apparatus	chem.	chemical
approx.	approximate (adj.), approximately	<i>C.I.</i>	<i>Colour Index</i> no.
		cks.	centistokes
aq.	aqueous	c.l.	car lots
Ar	aryl	cm.	centimeter(s)
ar-	aromatic; as, <i>ar</i> -derivatives of tetrahydronaphthalene	coeff.	coefficient
		com.	commercial
		compd.	compound (noun)
as-	asymmetric; as, <i>as-m</i> -xyldine	compn.	composition
		concd.	concentrated
ASA	American Standards Association	concn.	concentration
		cond.	conductivity
A.S.M.	American Society for Metals	const.	constant
		cor.	corrected

c.p.	chemically pure	ff.	following (pages)
cps.	centipoise	fl.oz.	fluid ounce(s)
crit.	critical	f.o.b.	free on board
cryst.	crystalline	f.p.	freezing point
crystd.	crystallized	ft.	foot (feet)
crystn.	crystallization	ft.-lb.	foot-pound(s)
cu.	cubic	g.	gram(s)
d (as, $d_+^{20}$ )	density (conveniently, specific gravity)	gal.	gallon(s)
$d$	differential operator	g.p.d.	grams per denier
$d$ -	<i>dextro</i> -, dextrorotatory	g.p.m.	gallons per minute
$D$ -	denoting configurational relationship, as to <i>dex</i> - <i>tro</i> -glyceraldehyde	hp.	horsepower
		hr.	hour(s)
		hyd.	hydrated, hydrous
		i.	insoluble
		<i>i</i> -	inactive; as, <i>i</i> -methio- nine
d.c.	direct current		
dec., decomp.	decompose(s)	i.b.p.	initial boiling point
decompn.	decomposition	I.C.C.	Interstate Commerce Commission
deriv.	derivative		
detd.	determined	I.D.	inner diameter
detn.	determination	in.	inch(es)
diam.	diameter	insol.	insoluble
dielec.	dielectric (adj.)	I.P.T.	Institute of Petroleum Technologists
dil.	dilute		
distd.	distilled	I.U.	International Unit(s)
distn.	distillation	I.U.C.,	International Union of
$DL$ -, $dl$ -	racemic	I.U.P.A.C.	Chemistry, Interna- tional Union of Pure and Applied Chem- istry
dm.	decimeter		
$e$	electron		
ed.	edition, editor	j.	joule
elec.	electric, electrical	K.	Kelvin
elev.	elevated	$K$	dissociation constant
e.m.f.	electromotive force	Kev	kilo electron volt
eng.	engineering	kg.	kilogram(s)
eq.	equation	kg.-cal.	kilogram-calorie(s)
equil.	equilibrium	kv.	kilovolt(s)
equiv.	equivalent	kv.-amp.	kilovolt-ampere(s)
esp.	especially	kw.	kilowatt(s)
estd.	estimated	kw.-hr.	kilowatt-hour(s)
estn.	estimation	l.	liter(s)
e.s.u.	electrostatic unit(s)	$l$ -	<i>levo</i> -, levorotatory
e.u.	entropy unit(s)	$L$ -	denoting configurational relationship, as to <i>levo</i> -glyceraldehyde
e.v.	electron volt(s)		
expt.	experiment	lb.	pound(s)
exptl.	experimental	LC <sub>50</sub>	concentration lethal to 50% of animals tested
ext.	extract		
extd.	extracted		
extn.	extraction		
F.	Fahrenheit		
Fedl.	Federal		

l.e.l.	less than car lots	N.O.I.B.N.	not otherwise indexed
LD <sub>50</sub>	dose lethal to 50% of animals tested		by name
ln	logarithm (natural)	<i>o</i> -	ortho; as, <i>o</i> -xylene
log	logarithm (common)	<i>O</i> -	denoting attachment to oxygen; as, <i>O</i> -acetyl- hydroxylamine
m.	meter(s)		
<i>m</i> -	meta; as, <i>m</i> -xylene	O.D.	outer diameter
M	metal	oz.	ounce(s)
<i>M</i>	molar (as applied to concn.; not molal, which is written out)	p., pp.	page, pages
		<i>p</i> -	para; as, <i>p</i> -xylene
ma.	milliampere(s)	pos.	positive (adj.)
manuf.	manufacture	powd.	powdered
manufd.	manufactured	p.p.m.	parts per million
manufg.	manufacturing	ppt.	precipitate
max.	maximum	pptd.	precipitated
M.C.A.	Manufacturing Chem- ists' Association	pptn.	precipitation
m.c.f.	million cubic feet	prepd.	prepared
m.e., meq.	milliequivalent(s)	prepn.	preparation
mech.	mechanical	Pr. no.	Foreign Prototype no. (for dyes)
M.e.v.	million electron volts	p.s.i.(g.), (a.)	pound(s) per square inch (gage), (absolute)
mg.	milligram(s)		
m.g.d.	million gallons per day	pt.	point
min.	minimum; minute(s)	pts.	parts
misc.	miscellaneous	quad. pt.	quadruple point
mixt.	mixture	qual.	qualitative
ml.	milliliter(s)	quant.	quantitative
M.L.D.	minimum lethal dose	<i>q.v.</i>	"which see"
mm.	millimeter(s)	R	univalent hydrocarbon radical (or hydrogen)
mM	millimole(s)		
mol.	molecule, molecular	R.	Rankine
m.p.	melting point	ref.	reference
m.p.h.	miles per hour	resp.	respectively
M.R.	molar refraction	r.h.	relative humidity
mv.	millivolt(s)	<i>R.I.</i>	<i>Ring Index</i> no.
mμ	millimicron(s)	r.p.m.	revolutions per minute
<i>n</i> (as, <i>n</i> <sub>D</sub> <sup>20</sup> )	index of refraction (for 20°C. and sodium light)	r.p.s.	revolutions per second
		s.	soluble
		<i>s</i> -	symmetric(al); as, <i>s</i> - <i>m</i> - xyldine
<i>n</i> -	normal; as, <i>n</i> -butyl		
<i>N</i>	normal (as applied to concn.)	<i>S</i> -	denoting attachment to sulfur; as, <i>S</i> -methyl- cysteine
<i>N</i> -	denoting attachment to nitrogen; as, <i>N</i> -meth- ylaniline	S.A.E.	Society of Automotive Engineers
neg.	negative (adj.)	satd.	saturated
no.	number	satn.	saturation

S.C.F.	standard cubic foot (feet)	t.s.i.	tons per square inch
		Twad.	Twaddell
Sch.	Schultz no. (for dyes)	u.v.	ultraviolet
sec.	second(s)	v.	volt(s)
sec-	secondary; as, <i>sec</i> -butyl	var.	variety
S.F.s.	Saybolt Furol second(s)	vic-	vicinal; as, <i>vic-m</i> -xyli-
sl.s.	slightly soluble		dine
sol.	soluble	vol.	volume(s) (not volatile)
soln.	solution	v.s.	very soluble
soly.	solubility	w.	watt(s)
sp.	specific	wt.	weight
sp., spp.	species	X.U. (10 <sup>-10</sup>	X-unit
spec.	specification	mm.)	
sp.gr.	specific gravity	yd.	yard(s)
sq.	square	yr.	year(s)
S.T.P.	standard temperature and pressure	[ $\alpha$ ] <sub>D</sub> <sup>20</sup>	optical rotation (for 20 °C. and sodium light)
subl.	sublime(s), subliming		
S.U.s.	Saybolt Universal second(s)	$\gamma$ $\partial$	microgram(s) differential operator
<i>sym</i> -	symmetric(al); as, <i>sym</i> - <i>m</i> -xylidine	$\Delta$	(partial) finite difference
T.A.P.P.I.	Technical Association of the Pulp and Paper Industry	$\eta$ $\lambda$ $\mu$	viscosity wave length micron(s)
tech.	technical	$\Omega$	ohm(s)
temp.	temperature	<	less than
<i>tert</i> -	tertiary; as, <i>tert</i> -butyl	>	more than
theoret.	theoretical	$\sim$	cycle(s)
t.p.h.	tons per hour	$\approx$	approximately equal to

Other letter symbols may be found in "Standard System of Nomenclature for Chemical Engineering Unit Operations" adopted by the American Institute of Chemical Engineers.

## SHIPPING REGULATIONS

Complete information for the U.S. is given in "Tariff No. 9 Publishing Interstate Commerce Commission Regulations for Transportation of Explosives and Other Dangerous Articles by Land and Water in Rail Freight Service and by Motor Vehicle (Highway) and Water Including Specifications for Shipping Containers," with supplements, issued by H. A. Campbell, Agent, 30 Vesey Street, New York 7, N.Y. (1954). The following terms for labeling explosives and other dangerous articles have been used in the Encyclopedia:

Red label (for inflammable liquids)  
 Yellow label (for inflammable solids and oxidizing materials)  
 White label (for acids and corrosive liquids)  
 Red label (for inflammable compressed gases)  
 Green label (for noninflammable compressed gases)  
 N.O.I.B.N. (not otherwise indexed by name)

In the text of the Encyclopedia the preferred terms "flammable" and "nonflammable" are used in place of "inflammable" and "noninflammable," respectively.

## STANDARD REFERENCE WORKS

The titles of the following reference works have usually been abbreviated when they are given in the bibliographies. See also *Literature of chemical technology*, Vol. 8, p. 418.

- Adams, R. (ed.), *Organic Reactions*, Wiley, N.Y., 7+ Vols., 1942-.
- Allen, A. H., *Commercial Organic Analysis*, 5th ed., Blakiston, New York, Vols. I-X, 1923-33.
- American Association of Textile Chemists and Colorists (A.A.T.C.C.), *1954 Technical Manual and Year Book*, Howes Pub. Co., N.Y., 1954.
- American Society for Testing Materials, *1952 Book of A.S.T.M. Standards*, Philadelphia, 7 Parts, 1952-53.
- American Standards Association (ASA), *American Standards*, N.Y.
- Annual Tables of Constants and Numerical Data*, C. Marie (ed.), McGraw-Hill, N.Y., 1912-34.
- Association of Official Agricultural Chemists (A.O.A.C.), *Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists*, 7th ed., Collegiate Press, Menasha, Wis., 1950.
- Badger, W. L., and McCabe, W. L., *Elements of Chemical Engineering*, 2nd ed., McGraw-Hill, N.Y., 1936.
- Beilstein, F. K., *Handbuch der organischen Chemie*, 4th ed., Springer, Berlin and Heidelberg, 71+ Vols., 1918-. (64 Vols. photo-lithoprinted by Edwards Bros., Ann Arbor, Mich.)
- Brauer, G. (ed.), *Handbuch der präparativen anorganischen Chemie*, Enke, Stuttgart.
- Clark, B. L., and Kolthoff, I. M. (eds.), *Chemical Analysis*, Interscience, N.Y., 7+ Vols., 1945-.
- Cook, E. F., and Martin, E. W. (eds.), *Remington's Practice of Pharmacy*, 9th ed., Mack Pub. Co., Easton, Penna., 1948.
- Elderfield, R. C. (ed.), *Heterocyclic Compounds*, Wiley, N.Y., 6 Vols., 1950-.
- Faith, W. L., Keyes, D. B., and Clark, R. L., *Industrial Chemicals*, Wiley, N.Y., 1950.
- Friedländer, P., *Fortschritte der Teerfarbenfabrikation und verwandter Industriezweige*, Springer, Berlin, Vols. I-XXV, 1888-1942.
- Friend, J. N. (ed.), *Textbook of Inorganic Chemistry*, Griffin, London, Vols. I-XI, 1914-38.
- Gmelins Handbuch der anorganischen Chemie*, 8th ed., Verlag Chemie, Weinheim/Bergstrasse, System-Nummern 1-70, 1924-.
- Great Britain General Medical Council, *British Pharmacopæia*, Constable, London, 1948; Addendum, 1951.
- Handbook of Chemistry and Physics*, C. D. Hodgman (ed.), 36th ed., Chem. Rubber Pub. Co., Cleveland, 1954.
- Heilbron, I. M., and Bunbury, H. M., *Dictionary of Organic Compounds*, Oxford Univ. Press, N.Y., Vols. I-IV, new rev. ed., 1953.
- Houben, J. (ed.), *Methoden der organischen Chemie (Weyls Methoden)*, 3rd ed., Thieme, Leipzig, Vols. I-IV, 1925-41. (Photo-lithoprinted by Edwards Bros., Ann Arbor, Mich.) For new edition see under Müller, E.
- Houben, J., *Fortschritte der Heilstoffchemie*. Erste Abteilung: *Das deutsche Patentschriftwesen*, Vols. I-VI; Zweite Abteilung: *Die Ergebnisse der wissenschaftlichen Literatur*, Vols. I-III; de Gruyter, Berlin, 1926-39. (Photo-lithoprinted by Edwards Bros., Ann Arbor, Mich.)
- Huntress, E. H., *Organic Chlorine Compounds*, Wiley, N.Y., 1948.
- Inorganic Syntheses*, McGraw-Hill, N.Y., 4+ Vols., 1939-.
- International Critical Tables of the Numerical Data of Physics, Chemistry, and Technology* (I.C.T.), E. W. Washburn (ed.), McGraw-Hill, N.Y., Vols. I-VIII, 1926-33.

- Landolt-Börnstein, *Physikalisch-chemische Tabellen*, 5th ed., Springer, Berlin, 8 Vols., 1923-36 (photo-lithoprinted by Edwards Bros., Ann Arbor, Mich.); 6th ed., *Zahlenwerte und Funktionen aus Physik, Chemie, Astronomie, Geophysik, Technik*, A. Eucken (ed.), Vols. I-IV, 1950-.
- Lange, N. A., and Forker, G. M. (eds.), *Handbook of Chemistry*, 8th ed., Handbook Publishers, Sandusky, Ohio, 1952.
- Lunge, G., and Berl, E., *Chemisch-technische Untersuchungsmethoden*, 8th ed., Springer, Berlin, 8 Vols., 1931-40. (Photo-lithoprinted by Edwards Bros., Ann Arbor, Mich.)
- Mark, H., Marvel, C. S., Melville, H. W., and Whitby, G. S. (eds.), *High Polymers*, Interscience, N.Y., 8+ Vols., 1940-.
- Mellor, J. W., *Comprehensive Treatise on Inorganic and Theoretical Chemistry*, Longmans, Green, N.Y., Vols. I-XVI, 1922-37.
- Merck Index, *The*, 6th ed., Merck & Co., Inc., Rahway, N.J., 1952.
- Müller, E. (ed.), *Methoden der organischen Chemie (Houben-Weyl)*, 4th ed., Thieme, Stuttgart, approx. 12 Vols., 1952-.
- National Formulary, The*, 9th ed. (N.F. IX), Committee on National Formulary, American Pharmaceutical Association, Washington, D.C., 1950.
- New and Nonofficial Remedies—1954* (N.N.R.) (1954); *Tests and Standards for New and Nonofficial Remedies* (1953); Council on Pharmacy and Chemistry of the American Medical Association, Lippincott, Philadelphia.
- Organic Syntheses*, Wiley, N.Y., Collective Vol. I (Vols. I-IX), 2nd ed., 1941; Collective Vol. II (Vols. X-XIX), 1943; Vols. XX-, 1940-.
- Osol, A., and Farrer, G. E., Jr., et al., *The Dispensatory of the United States of America* (U.S.D.), 24th ed., Lippincott, Philadelphia, 1947; Supplement, 1950.
- Palache, C., Berman, H., and Frondel, C., *Dana's System of Mineralogy*, 7th ed., Wiley, N.Y., 3 Vols., 1944-.
- Patterson, A. M., and Capell, L. T., *The Ring Index (R.I.)*, Reinhold, N.Y., 1940.
- Perry, J. H. (ed.), *Chemical Engineers' Handbook*, 3rd ed., McGraw-Hill, N.Y., 1950.
- Pharmacopœia of the United States of America, The* (*The United States Pharmacopœia*), 14th revision (U.S.P. XIV), United States Pharmacopœial Convention, Mack Pub. Co., Easton, Penna., 1950.
- Radt, F. (ed.), *Elsevier's Encyclopædia of Organic Chemistry*, Elsevier, Houston, Texas, and Amsterdam, 20 Vols., 1946-.
- Richter, V. von, *Chemistry of the Carbon Compounds*, 3rd ed. (trans. from 12th German ed.), Elsevier, Houston, Texas, and Amsterdam, Vols. I-IV, 1934-47.
- Rodd, E. H. (ed.), *Chemistry of Carbon Compounds*, Elsevier, Houston, Texas, and Amsterdam, Vols. I-V, 1952-.
- Rowe, F. M. (ed.), *Colour Index (C.I.)*, 1st ed., Society of Dyers and Colourists, Bradford, Yorkshire, 1924; Supplement, 1928.
- Schultz, G., and Lehmann, L., *Farbstofftabellen* (Sch.), 7th ed., Akadem. Verlag, Leipzig, 4 Vols., 1931-39. (Photo-lithoprinted by Edwards Bros., Ann Arbor, Mich.)
- Scott, W. W., *Standard Methods of Chemical Analysis*, Furman, N. H. (ed.), 5th ed., Van Nostrand, N.Y., Vols. I-II, 1939.
- Seidell, A., *Solubilities*. Vol. I: *Solubilities of Inorganic and Metal Organic Compounds*; Vol. II: *Solubilities of Organic Compounds*; Vol. III: *Supplement to Volumes I and II*; 3rd ed., Van Nostrand, N.Y., 1940-52.
- Sidgwick, N. V., *The Chemical Elements and Their Compounds*, Oxford Univ. Press, London, Vols. I-II, 1950.
- Thorpe's Dictionary of Applied Chemistry*, 4th ed., Longmans, Green, N.Y., 12 Vols., 1937-.
- Ullmann, F., *Enzyklopädie der technischen Chemie*, 2nd ed., Urban & Schwarzenberg, Vienna, 11 Vols., 1928-32 (photo-lithoprinted by Edwards Bros., Ann Arbor, Mich.); 3rd ed., 14 Vols., 1951-.
- Walker, W. H., Lewis, W. K., McAdams, W. H., and Gilliland, E. R., *Principles of Chemical Engineering*, 3rd ed., McGraw-Hill, N.Y., 1937.
- Weissberger, A. (ed.), *Technique of Organic Chemistry*, Interscience, N.Y., 8+ Vols., 1948-.
- Weissberger, A. (cons. ed.), *The Chemistry of Heterocyclic Compounds*, Interscience, N.Y., 8+ Vols., 1950-.

## PERIODICAL ABBREVIATIONS

The abbreviations used are, for the most part, those given in the "List of Periodicals Abstracted by Chemical Abstracts" (Vol. 45, No. 24, Pt. 2 (1951), also published separately). See also *Literature (survey)*, especially the sections on "Reviews, yearbooks, and monographs" and "Periodicals," Vol. 8, pp. 437-40.

<i>Am. Soc. Testing Materials, Proc.</i>	American Society for Testing Materials, Proceedings
<i>Anal. Chem.</i> (superseding <i>Ind. Eng. Chem., Anal. Ed.</i> )	Analytical Chemistry
<i>Angew. Chem.</i> (superseding <i>Die Chemie; Z. angew. Chem.</i> )	Angewandte Chemie
<i>Ann. Chem., Justus Liebig's</i>	Annalen der Chemie, Justus Liebig's
<i>Arch. Biochem. and Biophys.</i> (superseding <i>Arch. Biochem.</i> )	Archives of Biochemistry and Biophysics
<i>Arch. Ind. Hyg. and Occupational Med.</i> (superseding <i>J. Ind. Hyg. Toxicol.</i> )	Archives of Industrial Hygiene and Occupational Medicine
<i>Biochem. J. (London)</i>	Biochemical Journal, The
<i>Biochem. Z.</i>	Biochemische Zeitschrift
<i>Biochim. et Biophys. Acta</i>	Biochimica et Biophysica Acta
<i>BIOS Repts.</i>	British Intelligence Objectives Subcommittee Reports
<i>Bull. Chem. Soc. Japan</i>	Bulletin of the Chemical Society of Japan
<i>Bull. soc. chim. or Bull. soc. chim. France C.A.</i>	Bulletin de la société chimique de France
<i>Can. J. Research</i>	Chemical Abstracts
<i>Chem. Ber.</i> (superseding <i>Ber.</i> )	Canadian Journal of Research
<i>Chem. Eng.</i> (superseding <i>Chem. &amp; Met. Eng.</i> )	Chemische Berichte
<i>Chem. Eng. News</i> (superseding <i>News Ed. (Am. Chem. Soc.); Ind. Eng. Chem., News Ed.</i> )	Chemical Engineering with Chemical & Metallurgical Engineering
<i>Chem. Eng. Progress</i> (superseding <i>Trans. Am. Inst. Chem. Engrs.</i> )	Chemical and Engineering News
<i>Chem. Eng. Science</i>	Chemical Engineering Progress with Transactions of American Institute of Chemical Engineers
<i>Chemische Industrie</i>	Chemical Engineering Science
<i>Chemistry &amp; Industry</i> (formerly part of <i>J. Soc. Chem. Ind.</i> )	Chemische Industrie
<i>Chem. Revs.</i>	Chemistry & Industry
<i>Chem. Tech. (Berlin)</i> (superseding <i>Chem. Fabrik</i> )	Chemical Reviews
<i>Chem. Week</i> (superseding <i>Chem. Inds. Week</i> )	Chemische Technik, Die (Berlin)
<i>Chem. Zentr.</i>	Chemical Week
<i>Chem.-Ztg.</i>	Chemisches Zentralblatt
<i>Chimica e industria (Italy) or Chimica e industria (Milan)</i>	Chemiker-Zeitung mit dem Sonderteil, Die Chemische Praxis und der Beilage, Chemisch-technische Übersicht
<i>Chimie &amp; industrie</i>	Chimica, La, e l'industria (Italy) or (Milan)
<i>CIOS Repts.</i>	Chimie & industrie
<i>Compt. rend.</i>	Combined Intelligence Objectives Subcommittee Reports
<i>FIAT Repts.</i>	Comptes rendus hebdomadaires des séances de l'académie des sciences
<i>Fortschr. chem. Forsch.</i>	Field Information Agency Technical Reports
<i>Gazz. chim. ital.</i>	Fortschritte der chemischen Forschung
<i>Helv. Chim. Acta</i>	Gazzetta chimica italiana
	Helvetica Chimica Acta

- Ind. Chemist*  
*Ind. Eng. Chem.* (superseding *J. Ind. Eng. Chem.*)  
*J. Agr. Food Chem.*  
*J. Am. Chem. Soc.*  
*J. Am. Med. Assoc.*  
*J. Am. Pharm. Assoc.*  
*J. Appl. Chem. (U.S.S.R.)* (see also *Zhur. Priklad. Khim.*)  
*J. Appl. Phys.* (superseding *Physics*)  
*J. Assoc. Offic. Agr. Chemists*  
  
*J. Biol. Chem.*  
*J. Chem. Phys.*  
*J. Chem. Soc.*  
*J. Colloid Sci.*  
*J. Electrochem. Soc.* (superseding *Trans. Electrochem. Soc.*; *Trans. Am. Electrochem. Soc.*)  
*J. Gen. Chem. (U.S.S.R.)* (see also *Zhur. Obshch. Khim.*)  
*J. Indian Chem. Soc.*  
*J. Inst. Metals*  
  
*J. makromol. Chem.* (superseding *J. prakt. Chem.*)  
*J. Org. Chem.*  
*J. Phys. Chem.* (superseding *J. Phys. & Colloid Chem.*)  
*J. Polymer Sci.* (superseding *J. Polymer Research*)  
*J. Research Natl. Bur. Standards* (superseding *Bur. Standards J. Research*)  
*J. Sci. Food Agr.*  
*J. Soc. Chem. Ind. or J. Soc. Chem. Ind. (London)* (formerly containing *Chemistry & Industry*)  
*J. Soc. Chem. Ind., Japan*  
*Kolloid-Z.*  
*Mfg. Chemist*  
  
*Monatsh. Chem.*  
  
*Nature*  
*Nucleonics*  
*Office Tech. Services (OTS) Repts.* (superseding *Office Publication Board Repts.*)  
*Oil, Paint Drug Repr.*  
*Phys. Rev.*  
*Rec. trav. chim.*  
*Research (London)*  
*Revs. Mod. Phys.*  
*Science*  
*Trans. Am. Inst. Mining Met. Engrs.*  
  
*Trans. Am. Soc. Metals* (superseding *Trans. Am. Soc. Steel Treating*)  
*Trans. Inst. Chem. Engrs. (London)*  
  
*Z. anorg. u. allgem. Chem.* (superseding *Z. anorg. Chem.*)  
*Z. Elektrochem.*  
  
*Zhur. Obshch. Khim.*  
  
*Zhur. Priklad. Khim.*  
  
*Z. physik. Chem.*  
  
 Industrial Chemist and Chemical Manufacturer, The  
 Industrial and Engineering Chemistry  
  
 Journal of Agricultural and Food Chemistry  
 Journal of the American Chemical Society, The  
 Journal of the American Medical Association, The  
 Journal of the American Pharmaceutical Association  
 Journal of Applied Chemistry (U.S.S.R.)  
  
 Journal of Applied Physics  
 Journal of the Association of Official Agricultural Chemists  
 Journal of Biological Chemistry, The  
 Journal of Chemical Physics, The  
 Journal of the Chemical Society (London)  
 Journal of Colloid Science  
 Journal of the Electrochemical Society  
  
 Journal of General Chemistry (U.S.S.R.)  
  
 Journal of the Indian Chemical Society  
 Journal of the Institute of Metals and Metallurgical Abstracts  
 Journal für makromolekulare Chemie  
  
 Journal of Organic Chemistry, The  
 Journal of Physical Chemistry, The  
  
 Journal of Polymer Science  
  
 Journal of Research of the National Bureau of Standards  
 Journal of the Science of Food and Agriculture  
 Journal of the Society of Chemical Industry (London)  
  
 Journal of the Society of Chemical Industry, Japan  
 Kolloid-Zeitschrift  
 Manufacturing Chemist and Pharmaceutical and Fine Chemical Trade Journal Incorporating Manufacturing Perfumer  
 Monatshefte für Chemie und verwandte Teile anderer Wissenschaften  
 Nature  
 Nucleonics  
 Office of Technical Services Reports  
  
 Oil, Paint and Drug Reporter  
 Physical Review, The  
 Recueil des travaux chimiques des Pays-Bas  
 Research, A Journal of Science and Its Applications  
 Reviews of Modern Physics  
 Science  
 Transactions of the American Institute of Mining and Metallurgical Engineers  
 Transactions of the American Society for Metals  
  
 Transactions of the Institution of Chemical Engineers (London)  
 Zeitschrift für anorganische und allgemeine Chemie  
  
 Zeitschrift für Elektrochemie und angewandte physikalische Chemie  
 Zhurnal Obshch. Khimii (Journal of General Chemistry (U.S.S.R.))  
 Zhurnal Priklad. Khimii (Journal of Applied Chemistry (U.S.S.R.))  
 Zeitschrift für physikalische Chemie



# **S** *continued*

**STILBITE**,  $(\text{Na}_2, \text{Ca})\text{Al}_2\text{Si}_6\text{O}_{10} \cdot 6\text{H}_2\text{O}$ . See *Silica and silicates (mineral)*.

**STILLINGIA OIL**. See *Fats and fatty oils*, Vol. 6, pp. 144, 147.

## **STIMULANTS AND DEPRESSANTS OF THE NERVOUS SYSTEM**

Physiological Considerations.....	p. 1	Ganglionic Blocking Agents.....	p. 35
Central Nervous System Stimulants..	4	Skeletal Neuromuscular Blocking	
Central Nervous System Depressants..	6	Agents.....	37
Adrenergic Stimulants.....	18	Reflex Agents.....	41
Adrenergic Blocking Agents.....	22	Bibliography.....	42
Cholinergic Stimulants.....	27	Index.....	44
Muscarinic Blocking Agents.....	32		

See also *Alkaloids; Analgesics and antipyretics; Anesthetics; Antispasmodics; Barbituric acid and barbiturates; Cardiovascular agents; Choline; Emetics and expectorants; Epinephrine; Heterocyclic compounds; Histamine and antihistamine agents; Hypnotics and sedatives; Quaternary ammonium compounds.*

### **Physiological Considerations**

The nervous system of man and all other vertebrates includes both central and peripheral neuron networks. It is usually subdivided into:

- A. Central nervous system
- B. Peripheral nervous system
  1. Somatic or voluntary nervous system
  2. Autonomic or involuntary nervous system
    - a. Sympathetic division
    - b. Parasympathetic division

The *central nervous system* includes the cerebral cortex, brain stem, cerebellum, and spinal cord. All divisions of the peripheral nervous system contain both sensory (*afferent*) and motor (*efferent*) components. The *peripheral somatic nervous system* is composed of efferent nerves to skeletal (voluntary) muscle and afferent connections from superficial and deep receptors. The *autonomic nervous system* consists of efferent nerves, ganglia, and plexuses, which innervate the thoracic and abdominal viscera and widely distributed glands and blood vessels, as well as afferent fibers from most of the same areas.

## 2      *STIMULANTS AND DEPRESSANTS*

The autonomic nervous system is subdivided into sympathetic and parasympathetic divisions. The *sympathetic division*, including the adrenal medulla, is organized to elicit a diffuse response, whereas the *parasympathetic division* provides for more discrete and limited effects. Efferent pathways of both the sympathetic and the parasympathetic divisions have peripheral synapses and therefore pre- and postganglionic nerve fibers. All preganglionic nerve fibers and most postganglionic parasympathetic fibers are *cholinergic*; that is, they release an acetylcholine-like substance when stimulated. On the other hand, most sympathetic postganglionic fibers are *adrenergic*; that is, they release an epinephrine- or norepinephrine-like substance when stimulated.

In general, but not in all areas, the sympathetic and parasympathetic systems act as physiological antagonists (Table I). If one inhibits a certain function, the other stimulates it, and vice

TABLE I. Responses of Effector Organs to Chemical Mediators.

Organ	Adrenergic	Cholinergic
Heart		
Rate	Increase	Decrease
Output	Increase	Decrease
Blood vessels		
Coronary	Dilatation	Dilatation
Muscle	Dilatation or constriction	Dilatation
Cerebral	Constriction	Dilatation
Skin and visceral	Constriction	Dilatation
Eye		
Iris	Mydriasis	Miosis
Ciliary muscle	—	Stimulation
Skin		
Pilomotor muscles	Stimulation	—
Lung		
Bronchial muscle	Inhibition	Stimulation
Glands	No effect or slight stimulation	Stimulation
Gastrointestinal tract		
Motility and tone	Inhibition	Stimulation
Sphincters	Stimulation	Inhibition
Liver	Glycogenolysis	—
Urinary bladder		
Detrusor	Inhibition	Stimulation
Trigone and sphincter	Stimulation	Inhibition
Autonomic ganglia and adrenal medulla	Inhibition	Stimulation
Skeletal muscle	Facilitation	Stimulation

versa. Many organs are innervated by both systems, and their responses are the algebraic sum of the effects of both. Removing the effects of one system by extirpation or by drug blockade may produce the same response as augmenting the activity of the other. The effects of adrenergic (usually sympathetic) and cholinergic (usually parasympathetic) mediators are summarized in Table I. Responses to sympathetic and parasympathetic nerve stimulation are similar to those listed, but some organs, such as most blood vessels, are not innervated by parasympathetic fibers. (See also 3,4.)

From a functional point of view, the rigid anatomical division of the nervous system into central and peripheral components is artificial. Any voluntary movement involves neurons of the cerebral cortex which send axons down the brain stem and spinal cord to synapse with motor horn cells. The axons of these motor neurons then pass through peripheral somatic nerves to innervate skeletal muscles which execute the desired movement. Likewise most autonomic nervous system activity is dependent upon connections with many parts of the brain and spinal cord.

Drugs may act at many different sites within the nervous system. They may facilitate or inhibit transmission along nerve cells or across their junctions, and either stimulate or depress effector cells in such a way as to mimic increased or decreased nervous activity. An agent may be depressant

**TABLE II. Examples of Drugs Affecting the Nervous System.**

Primary site of action	Stimulants	Depressants <sup>a</sup>
Central nervous system	Picrotoxin Pentylentetrazol Nikethamide Sympathomimetics Carbon dioxide (low concn.) Strychnine Xanthines Camphor Semicarbazides Ammonium ion Fluoroacetate Anticholinesterases <sup>b</sup> Local anesthetics	Ethers Halogenated compounds Hydrocarbons Carbamates (urethan, etc.) Alcohols Barbiturates Ions (bromide, magnesium, etc.) Opiates and related drugs Hydantoins Oxazolidines Phenacetylureas Glycerol derivatives (mephensin, etc.) Benzazoles Ergot alkaloids Carbon dioxide (high concn.) Antihistaminics (diphenhydramine, etc.) Atropine and some other muscarinic blocking agents
Peripheral nervous system		
Nerve fibers	Calcium ion deficiency	Local anesthetics
Sensory receptors	Acetylcholine Histamine	Local anesthetics
Motor endplate	Choline derivatives (low dose) Nicotine (low dose) Anticholinesterases <sup>b</sup> Potassium ion	Choline derivatives (high dose) Nicotine (high dose) Tubocurarine and related alkaloids Synthetic quaternary nitrogen compounds (decamethonium, etc.) Magnesium ion
Autonomic nervous system		
Sensory receptors	Veratrum alkaloids Choline derivatives Nicotine Lobeline Cyanide ion	Ganglionic blocking agents (hexamethonium, etc.)
Motor ganglia	Choline esters and ethers (low dose) Anticholinesterases <sup>b</sup> Nicotine (low dose)	Choline esters (high dose) Sympathomimetics Nicotine (high dose) Tetraethylammonium Hexamethonium, etc. Solanaeous alkaloids
Effector cells innervated by postganglionic cholinergic nerves	Choline derivatives Anticholinesterases <sup>b</sup> Alkaloids (muscarine, pilocarpine, arecoline)	Synthetic antispasmodics (atropine, methantheline, etc.)
Effector cells innervated by postganglionic adrenergic nerves	Phenethylamines Pyrocatechol derivatives Aliphatic and alicyclic amines Some imidazolines	$\beta$ -Haloalkylamines Some ergot alkaloids Some imidazolines Benzodioxans Yohimbine and other alkaloids

<sup>a</sup> Includes blocking agents.

<sup>b</sup> Act indirectly by inhibiting cholinesterases.

at one level or locus and stimulant at another; for example, morphine depresses the cerebral cortex and respiratory center but augments certain spinal cord reflexes. Likewise autonomic agents such as epinephrine may excite certain effector cells and inhibit others. Excitatory and inhibitory systems interact complexly, both centrally and peripherally. Depression of a central inhibitory system may cause apparent stimulation due to the phenomenon of release; likewise stimulation of an inhibitory system may cause further inhibition. Peripherally, stimulation of carotid sinus pressoreceptors may reflexly depress medullary activity and cause a reduction in blood pressure and inhibition of respiration. It is apparent that any classification of drugs as stimulants or depressants of nervous function is subject to error. Such a classification cannot be accurate unless the locus and mechanism of the action of each drug is known, and this information is rarely available.

The ubiquity of substances which affect the nervous system or simulate alterations in nervous activity by direct actions on effector cells may be seen by inspection of the partial list presented in Table II.

Many of these substances have been described in part in other sections of this Encyclopedia, to which the reader will be referred in the text. As indicated in Table II, many drugs have more than one locus of action. Autonomic agents especially have diverse effects. For example, atropine not only blocks postganglionic parasympathetic responses but also acts on the brain stem. Similarly, epinephrine and its congeners act on effector cells innervated by postganglionic adrenergic nerve fibers and also on several areas of the central nervous system.

In the following sections, agents will be classified on the basis of their most obvious gross pharmacological effects. Most of the compounds discussed are employed as salts. However, the anions involved are of importance only in determining certain physical properties of the products. Consequently the pharmacology and the structure-activity relations of the various compounds will be presented without regard for the specific anions involved. The reader may assume that the discussion is applicable to all salts which are reasonably soluble in aqueous mediums.

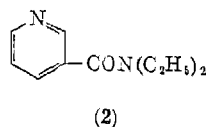
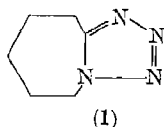
### Central Nervous System Stimulants

Many drugs produce excitation of the central nervous system, but relatively few of these are of therapeutic importance. Increased nervous activity induced by drugs is always followed by a period of depression proportional to the previous excitation. Because of this, the more powerful stimulants are used for relatively short periods of time, usually to stimulate the depressed respiratory center in emergencies. These agents are frequently referred to as analeptics because they reduce narcosis. (See 3,35.)

**Picrotoxin**, U.S.P. XIV, N.N.R.,  $C_{30}H_{34}O_{13}$ , is obtained from the East Indian fish-berry *Anamirta cocculus*. Its chemical structure has not been determined, but it seems to be an equimolecular compound of *picrotoxinin*,  $C_{16}H_{16}O_6$ , and *picrotin*,  $C_{14}H_{18}O_7$ ; the former is pharmacologically the more active. Picrotoxin is a powerful stimulant of the central nervous system, but even when administered intravenously it acts only after a latency of 10-30 minutes. The metabolic fate of this agent is unknown, but it rapidly leaves the circulation. A portion can be recovered in the urine. The predominant action of therapeutic doses of picrotoxin is stimulation of the respiratory center of the medulla. Larger doses affect cerebral centers and produce clonic convulsions with subsequent depression. Death may result from respiratory failure.

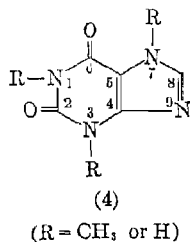
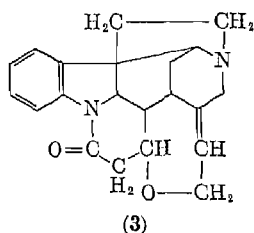
**Pentylenetetrazol**, U.S.P. XIV (6,7,8,9-tetrahydro-5-azepotetrazole, Metrazol, 1), is another potent central nervous system stimulant. In contrast to picrotoxin, it has a rapid onset of action when administered intravenously. Pentylenetetrazol is rapidly detoxified by the liver, and consequently the duration of action is relatively short; it is only weakly active after oral administration. The drug acts chiefly on

the respiratory center of the medulla but also affects higher brain centers. Subconvulsant doses in certain laboratory animals may produce an electroencephalographic pattern of "spike and dome" waves similar to those seen in petit mal epilepsy. Large doses produce tonic-clonic convulsions.



**Nikethamide**, U.S.P. XIV, N.N.R. (*N,N*-diethylnicotinamide, *Coramine*, 2) (see Vol. 9, p. 312) probably produces respiratory stimulation by a direct action on the medulla, although some action via peripheral chemoreceptors has been suggested. It is a less effective respiratory stimulant than are picrotoxin, pentylenetetrazol, or several sympathomimetics (see p. 20). When administered in large doses, it causes excitation of higher motor centers with subsequent convulsions. Postexcitatory depression is pronounced. Nikethamide does not have clinically significant cardiovascular effects, although trade names such as *Coramine* might imply otherwise. It can substitute for nicotinic acid or nicotinamide in nutritional deficiencies.

**Strychnine**, N.F. IX,  $C_{21}H_{22}N_2O_2$ , is the principal alkaloid obtained from seeds of the Indian tree *Strychnos nux vomica*. Its probable structure is as illustrated (3).



Strychnine stimulates all parts of the central nervous system but acts predominantly on the internuncial neurons of the spinal cord. It also depresses reciprocal reflex inhibition. In low doses strychnine increases reflex excitability, but after larger doses coordinated activity is lost and a simultaneous discharge of motor neurons to both flexor and extensor muscles occurs, giving rise to "spinal convulsions." Local application to any portion of the central nervous system causes increased excitability or spontaneous discharge of the part. This response has been used extensively in experiments designed to map out interconnections in the central nervous system.

The **methylated xanthines** (4), **caffeine**, U.S.P. XIV (1,3,7-trimethylxanthine), **theophylline**, U.S.P. XIV (1,3-dimethylxanthine), and **theobromine**, U.S.P. XIV, N. F. IX (3,7-dimethylxanthine), are widely distributed in plants whose aqueous extracts, such as coffee, tea, and cocoa, are used as beverages. (See also Vol. 1, p. 475; *Caffeine*; *Cardiovascular agents*, Vol. 3, p. 221; *Diuretics*, Vol. 5, p. 191.) The popularity of these beverages can be attributed in part to their mild central stimulant actions. Methylated xanthines also have other important pharmacological effects, including cardiac and skeletal muscle stimulation and a diuretic action. The phar-

macological properties of the several methylated xanthines are qualitatively similar, but they vary in the relative intensity of their effects on different systems. Caffeine is the most active as a central nervous system stimulant, but all are much weaker than agents such as picrotoxin or pentylenetetrazol. In small doses the methylated xanthines stimulate the higher nervous centers. With increasing dosage the medulla and spinal cord are also affected, and very large doses may produce tonic-clonic convulsions.

#### USES OF CENTRAL NERVOUS SYSTEM STIMULANTS

With the exception of strychnine, all the substances discussed above are used therapeutically to stimulate respiration. Such stimulation may be useful as an emergency measure in the treatment of severe central nervous system depression, particularly in cases of respiratory depression due to drugs such as the barbiturates. For prolonged analeptic effects picrotoxin or one of the sympathomimetics may be employed. Pentylenetetrazol may be used where a rapidly acting, potent analeptic is needed. It has, however, a short duration of action. Perhaps the safest analeptics, but also the least potent, are the xanthines. The use of potent analeptics is contraindicated in morphine poisoning because these agents act synergistically with morphine at certain levels of the central nervous system. Pentylenetetrazol has been employed in the convulsive shock therapy of certain mental disorders, but this use is diminishing because of the frightening aura which precedes the seizure, and because the drug is more difficult to control than is electroshock. Formerly, very small doses of strychnine were used as a "tonic," but at present the drug is used only as an ingredient of animal poisons.

#### Central Nervous System Depressants

In contrast to the small number of therapeutically useful central nervous system stimulants, there are many important central nervous system depressants. These may be classified as:

- (1) General anesthetics: nitrous oxide, ether, ethylene, cyclopropane, etc.
- (2) Alcohols, particularly ethyl alcohol.
- (3) Sedatives and soporifics: barbiturates, chloral hydrate, paraldehyde, etc.
- (4) Interneuron depressants: mephenesin, benzazoles, etc.
- (5) Narcotic analgesics: morphine, its congeners, and related drugs.
- (6) Antipyretic analgesics: salicylates, aminopyrine, etc.
- (7) Anticonvulsants: diphenylhydantoin, trimethadione, phenacemide, etc.
- (8) Miscellaneous depressants.

#### GENERAL ANESTHETICS

Many chemically unrelated compounds (Table III) produce a fairly consistent pattern of general anesthesia, depressing in sequence cortex, brain stem, spinal cord, and medulla (3,7). Death results from respiratory center depression. Numerous theories of the mechanism of anesthesia based on the physical or chemical properties of the anesthetics have been proposed. These include the lipid solubility, surface tension, permeability, colloid, enzymic, and electrical theories (23). All may be valid in part, but none is supported by convincing evidence. Because of the wide diversity

of chemicals which produce general anesthesia, no simple relation between chemical structure and anesthetic activity is apparent. However, a few important factors are known. Compounds with two-carbon radicals are potent central nervous system depressants and are relatively nontoxic. Introduction of an ether linkage increases potency, as does unsaturation. Chlorine or bromine substitutions in alkyl groups increase potency but also increase toxicity for organs such as the liver, kidney, and heart. See also *Anesthetics*.

The pattern of general anesthesia consists of an irregular depression of the cerebro-spinal axis, converging toward the medulla. The depth of anesthesia is arbitrarily divided into four stages which are defined on the basis of the extent to which depression

TABLE III. Properties of Some General Anesthetics.

Agent	Physical character	Approximate anesthetic concentration or dose <sup>a</sup>	Approximate lethal concentration or dose	Comments	Status
Nitrous oxide	Gas	90%	Anoxia	Only for light surgical anesthesia; little toxicity.	U.S.P. XIV
Ethylene	Gas	85%	Anoxia	Only for light to moderate surgical anesthesia; little toxicity.	U.S.P. XIV
Cyclopropane	Gas	15%	40%	Excellent anesthetic in hands of experienced; sensitizes heart to epinephrine.	U.S.P. XIV, N.N.R.
Ethyl ether	Liquid → vapor	4%	7%	Safe, reliable general anesthetic; postoperative distress common.	U.S.P. XIV, N.F. IX
Chloroform	Liquid → vapor	1.5%	2%	Produces liver and kidney damage; sensitizes heart to epinephrine.	U.S.P. XIV, N.F. IX
Vinyl ether	Liquid → vapor	1%	3%	Used for rapid induction and short operative procedures; produces liver damage.	U.S.P. XIV, N.F. IX
Ethyl chloride	Liquid → vapor	3%	6%	Produces liver damage; sensitizes the heart to epinephrine; low margin of safety.	U.S.P. XIV
Trichloroethylene	Liquid → vapor	5%	10%	Used primarily as an analgesic agent; may produce liver damage.	U.S.P. XIV
Tribromoethanol	Crystalline solid	80 mg./kg. <sup>b</sup>	200 mg./kg.	Used as basal anesthetic only; no adequate control once given; may produce liver damage.	U.S.P. XIV, N.N.R.
Thiopental	Crystalline solid	15-30 mg./kg.	30-50 mg./kg.	Given intravenously for induction of anesthesia and for short operative procedures; dose dependent on rate of administration.	U.S.P. XIV, N.N.R.

<sup>a</sup> Without preanesthetic medication.

<sup>b</sup> For basal anesthesia.

has progressed (3,42). These stages are: (1) stage of analgesia or altered consciousness (cortical depression); (2) stage of delirium or excitement (subcortical release); (3) stage of surgical anesthesia (brain stem and spinal cord depression); (4) stage of medullary paralysis. The anesthetic agent used and the speed of induction of anesthesia modify the appearance of the various stages. All the stages can be observed clearly when ethyl ether or chloroform (*q.v.*) is employed. However, the more rapid induction with ethylene, vinyl ether, or cyclopropane obscures some stages, and intravenous anesthetics such as the thiobarbiturates may produce unconsciousness and surgical anesthesia without obvious intermediate stages. The most potent volatile and gaseous anesthetics, including **ethyl ether**, **vinyl ether**, **chloroform**, and **cyclopropane** (Table III), produce medullary depression in concentrations that allow adequate oxygenation. They are referred to as 100% anesthetics. **Nitrous oxide** and **ethylene** are much less potent and cannot produce the deeper stages of anesthesia in concentrations which allow for 20% or more of oxygen. Excitement, a high metabolic rate, and similar factors increase resistance to anesthetic agents. Consequently sedatives (p. 9) and narcotics (p. 12) are usually administered prior to a general anesthetic to reduce apprehension and central nervous system excitability. Adequate preanesthetic medication allows agents such as ethylene to be used for most types of general surgery. In addition, skeletal neuromuscular blocking drugs (p. 37) are frequently employed to supplement the weaker general anesthetics, or to reduce the concentration of other anesthetics required to produce adequate muscular relaxation.

#### ALCOHOLS

The pharmacological actions of the alcohols (*q.v.*) are much more diverse than those of the hydrocarbons from which they are derived. In general, the alcohols are central nervous system depressants. Increasing the chain length of simple primary alcohols to 6 or 8 carbon atoms increases potency, while further increasing the chain length gradually reduces activity;  $C_{16}$  alcohols are essentially inert. Branched-chain primary alcohols are more potent central nervous system depressants than isomeric normal alcohols, and secondary and tertiary alcohols are still more active in ascending order. Unsaturation also increases depressant properties. In general, polyhydroxy alcohols are considerably less depressant than comparable monohydroxy compounds. With the exception of methanol, depressant potency and toxicity are roughly parallel throughout the alcohol group. Methanol has a relatively low acute depressant activity, but its metabolic products are highly toxic. (See 86.)

Among the simple alcohols, **ethyl alcohol**, U.S.P. XIV, N.F. IX, is the safest central nervous system depressant. It produces the same type of irregular descending depression of the nervous system as the general anesthetics, and in large doses it can produce surgical anesthesia. However, it is not used for this purpose because it has a small margin of safety. The apparent stimulation or euphoria produced by small amounts of ethyl alcohol is due to depression of the cerebral cortex with release of subcortical centers. Ethyl alcohol is oxidized to carbon dioxide and water to the extent of at least 90% and provides a source of readily utilized calories. The liver is the chief site of initial oxidation. **Tetraethylthiuram disulfide** (bis(diethylthiocarbamoyl) disulfide, Disulfiram, Antabuse, N.N.R.),  $[(C_2H_5)_2NCS]_2S_2$ , blocks the oxidation of ethyl alcohol at the acetaldehyde stage. Thus a patient pretreated with tetraethylthiuram disulfide who ingests ethyl alcohol will develop an unpleasant reaction characteristic of acetaldehyde (49). This reaction has been exploited in the therapy of

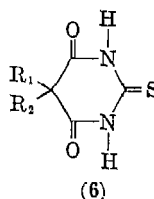
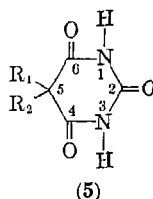


chronic alcoholism. It is potentially dangerous, particularly if large amounts of alcohol are taken. **Methanol** (*q.v.*), N.F. IX, is oxidized in the body to formaldehyde and formic acid. These oxidation products are largely responsible for the toxicity of methanol, which is characterized by initial inebriation followed by visual disturbances and coma. Death occurs from respiratory paralysis and frequently may be prevented by the administration of adequate amounts of sodium bicarbonate or other base.

Ethyl alcohol produces vasodilatation, and this property has received some clinical application in the treatment of vascular disease. The response is more predictable after intravenous infusion than after oral administration. Ethyl and isopropyl alcohols are widely used as antiseptics, and the former is a common vehicle for a wide variety of drugs. The toxicity of the longer-chain alcohols is too great to warrant their systemic use.

#### SEDATIVES AND SOPORIFICS

The **barbiturates** are important central nervous system depressants which are widely used as sedatives, soporifics, and general anesthetics. (See also *Barbituric acid and barbiturates*; and *Hypnotics and sedatives*.) All important members of this series are 5,5-disubstituted barbituric (5) or 2-thiobarbituric acids (6) (see 82). Barbituric acid itself and the 5-monoalkylbarbituric acids are devoid of soporific proper-



ties. An increase (up to 5 carbons) in the length of a 5-alkyl substituent increases potency but decreases duration of action. Beyond 5 carbons, depressant potency is decreased and convulsant properties appear. Alkyl substituents on both nitrogen atoms also tend to contribute convulsant properties. Barbiturates with *n*-alkyl radicals have a longer duration of action than those with complex ring or branched-chain substituents. Unsaturation of the side chain increases potency. The thiobarbiturates have an ultrashort action, largely because they are rapidly removed from the blood stream and deposited in fat (19).

The metabolic fate of the barbiturates depends upon their chemical structure. Agents with more complex substituents (amobarbital, pentobarbital, hexobarbital, etc.) and the thiobarbiturates are primarily metabolized, while barbital and to a lesser extent phenobarbital are excreted in the urine. The various 5,5-disubstituted barbituric acid derivatives differ markedly in potency and in rate of onset and duration of action (Table IV).

Any degree of central depression from mild sedation to surgical anesthesia can be produced by the barbiturates. Most of these agents are useful to promote sleep. The choice of which agent to use for this purpose is dependent upon the duration of action desired. For example, if a patient has insomnia at bedtime, a barbiturate with a short duration of action will suffice; if the patient remains awake after arousing from a brief period of sleep, a barbiturate with an intermediate duration of action is

TABLE IV. Some Useful Barbituric Acid Derivatives.

Compound	Substitutions on barbituric acid ring			Duration of action (oral soporific dose)	Status
	Position 5		Other		
	R <sub>1</sub>	R <sub>2</sub>			
Barbital	Ethyl	Ethyl	—	Long	U.S.P. XIV, N.F. IX
Mephobarbital	Ethyl	Phenyl	1-Methyl	Long	N.N.R.
Phenobarbital	Ethyl	Phenyl	—	Long	U.S.P. XIV
Aprobarbital	Allyl	Isopropyl	—	Intermediate	N.N.R.
Butabarbital	Ethyl	1-Methylpropyl	—	Intermediate	N.N.R.
Diallylbarbital	Allyl	Allyl	—	Intermediate	—
Probarbital	Ethyl	Isopropyl	—	Intermediate	N.N.R.
Vinbarbital	Ethyl	1-Methyl-1-butenyl	—	Intermediate	N.N.R.
Amobarbital	Ethyl	Isoamyl	—	Short	N.F. IX
Cyclobarbital	Ethyl	Cyclohexenyl	—	Short	—
Hexethal	Ethyl	<i>n</i> -Hexyl	—	Short	N.N.R.
Pentobarbital	Ethyl	1-Methylbutyl	—	Short	U.S.P. XIV, N.F. IX, N.N.R.
Secobarbital	Allyl	1-Methylbutyl	—	Short	N.N.R.
Hexobarbital	Methyl	Cyclohexenyl	1-Methyl	Ultrashort <sup>a</sup>	N.N.R.
Thiamylal	Allyl	1-Methylbutyl	2-Thio	Ultrashort <sup>a</sup>	N.N.R.
Thiopental	Ethyl	1-Methylbutyl	2-Thio	Ultrashort <sup>a</sup>	U.S.P. XIV, N.N.R.

<sup>a</sup> Anesthetic dose given intravenously.

Source: N.N.R. 1953, p. 247.

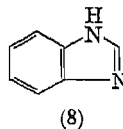
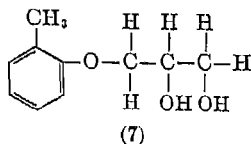
prescribed. Similarly, an agent with a long duration of action, for example, phenobarbital, is prescribed when mild continuous sedation is desirable.

All the barbiturates are anticonvulsant in anesthetic doses, but the **5-phenyl derivatives** such as **phenobarbital** are unique in that they exert anticonvulsant effects in doses which do not greatly depress the normal activity of the central nervous system. For this reason they are used extensively in the symptomatic treatment of grand mal epilepsy, frequently in combination with other agents (p. 15). **Mephobarbital** (Mebaral) is claimed to produce less sedation than phenobarbital, but its anticonvulsant activity is also less. Barbiturates with an ultrashort duration of action are used as intravenous anesthetics. They are very useful for short operations and are ideal for inducing anesthesia prior to the more prolonged use of other general anesthetics.

Miscellaneous sedatives and soporifics include paraldehyde, U.S.P. XIV, chloral hydrate, U.S.P. XIV, sulfones (*q.v.*), urethan, U.S.P. XIV, etc. See *Hypnotics and sedatives*.

#### INTERNEURON DEPRESSANTS

The discovery that agents such as **mephenesin**, N.N.R. (3-*o*-toloxy-1,2-propanediol, Myanesin, **7**), and **benzimidazole** (**8**) act predominantly upon interneurons of the central nervous system established a new class of depressants (15). Other cen-

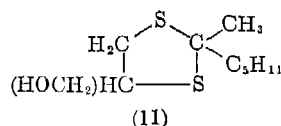
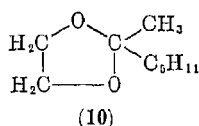
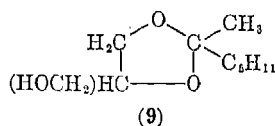


tral depressants, such as ether or a barbiturate, inhibit transmission over both mono- and polysynaptic neuronal pathways. Mephenesin and similar agents, on the other hand, selectively depress polysynaptic pathways because these involve one or more interneurons. This depression of interneurons is accompanied by an ascending reversible paralysis of skeletal muscle; extensive skeletal muscle relaxation may be obtained.

Therapeutic doses of mephenesin produce some muscular relaxation and slight sedation. The drug is used principally in the treatment of spasticity, but its relatively short duration of action is a serious limitation. This has spurred the search for more potent and longer-acting substitutes. A number of monoethers of glycerol have pharmacological properties similar to those of mephenesin, but none is superior (15).

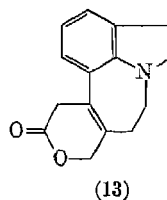
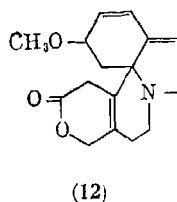
Several **propanediols**, of which **Prenderol** (2,2-diethyl-1,3-propanediol, DEP),  $\text{HOCH}_2\text{C}(\text{C}_2\text{H}_5)_2\text{CH}_2\text{OH}$ , is the most useful, are also interneuron depressants (39). However, their very short duration of action greatly limits their usefulness.

**Glyketal** (2-methyl-2-*n*-amyl-4-hydroxymethyl-1,3-dioxolane, **9**) is another interneuron depressant with properties similar to those of the glycerol ethers. Among



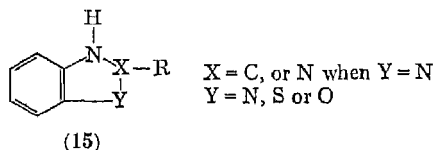
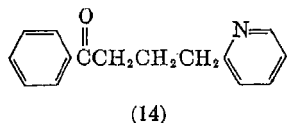
congeners of glyketal which have been investigated, the presence of a free hydroxyl group appears to be essential for activity. Removal of the hydroxyl group (**10**) or its acetylation abolishes or markedly decreases paralyzing potency. The dithiolane analog (**11**) is inactive, as are 4-hydroxymethyl-1,3-dioxolanes which contain a nitrogen atom in the 2-substituent (15).

**$\beta$ -Erythroidine** (**12**) (see Vol. 1, p. 491) is a tertiary amine which depresses the central nervous system in addition to an action on the neuromuscular junction (p. 39). A derivative, **apo- $\beta$ -erythroidine** (**13**), obtained by heating  $\beta$ -erythroidine to  $120^\circ\text{C}$



with either phosphoric or sulfuric acid, is devoid of neuromuscular blocking activity but selectively depresses the spinal cord and induces the reversible ascending paralysis characteristic of interneuron depressants (74). Several synthetic **pyridine derivatives**, of which **4-(2-pyridyl)butyrophenone** (EJA II, **14**) is the most potent, also possess interneuron depressant activity (77).

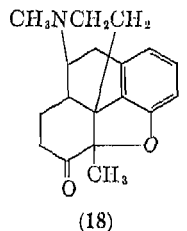
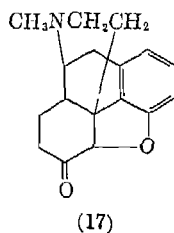
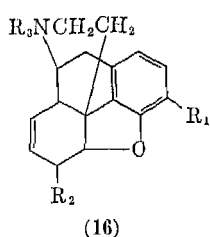
A number of **benzazoles** (**15**, see also *Heterocyclic compounds*) in addition to benzimidazole are known to be interneuron depressants. Paralyzing doses of these



agents do not affect peripheral nerve or transmission across the neuromuscular junction. Substituted **2-aminobenzothiazoles** are particularly potent interneuron depressants (31,38). However, none of these agents studied to date is sufficiently free of side effects to have therapeutic merit.

#### NARCOTIC ANALGESICS

The narcotic analgesics differ from other central nervous system depressants in that they alleviate pain in doses which do not impair consciousness, and produce physical dependence when administered chronically. They are much more effective in relieving pain than antipyretic analgesics such as the salicylates or aminopyrine. The opium alkaloids (16) have been used for centuries. In recent years several synthetic substitutes have been introduced into therapeutics, but the relative merits of the



natural and synthetic compounds have not as yet been fully determined. The use of all narcotic analgesics is regulated by the provisions of the Harrison Narcotic Act. See Table V; see also *Analgesics and antipyretics*.

**Opium Alkaloids and Derivatives.** (See Vol. 1, p. 491.) The classical narcotic analgesic is **morphine**, U.S.P. XIV, N.F. IX (16). Its actions on the nervous system

TABLE V. Opium Alkaloids and Derivatives.

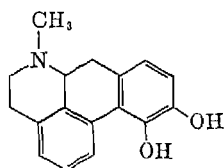
Agent	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>
Morphine	OH	OH	CH <sub>3</sub>
Nalorphine	OH	OH	CH <sub>2</sub> CH=CH <sub>2</sub>
Codeine	OCH <sub>3</sub>	OH	CH <sub>3</sub>
Ethylmorphine	OC <sub>2</sub> H <sub>5</sub>	OH	CH <sub>3</sub>
Heroin	OOCCH <sub>3</sub>	OOCCH <sub>3</sub>	CH <sub>3</sub>

are a complex mixture of stimulation and depression (54). There are marked species differences in the overt response to morphine. The dog, monkey, and man are primarily depressed, but the cat is excited. In man the threshold for painful stimuli is increased; sensation is not abolished, but pain is made more tolerable. Respiratory depression may be severe, and toxic doses kill by producing respiratory arrest. Morphine also has many peripheral effects and may induce a fall in blood pressure and spastic immobility of the gastrointestinal tract. Tolerance and physical dependence develop with continuous administration, and a characteristic withdrawal syndrome develops after cessation of chronic administration. A derivative of morphine, **nalorphine**, N.N.R. (*N*-allylnormorphine, Nalline, 16), is a potent antagonist to most actions of morphine and other narcotic analgesics, and it provides a most effective treatment for the respiratory depression which is characteristic of overdosage with these agents (30,34). It

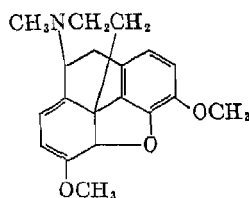
also induces an almost immediate appearance of the withdrawal syndrome when administered to tolerant animals or man (89).

**Codeine**, U.S.P. XIV, N.F. IX (methymorphine, 16), is a naturally occurring alkaloid with properties qualitatively similar to those of morphine. However, it is a less potent analgesic and produces less depression and euphoria. Many partially synthetic derivatives of morphine have been studied. **Ethylmorphine**, U.S.P. XIV (Dionine, 16), resembles codeine in its pharmacological effects. The diacetyl derivative (**heroin**, 16) is a much more potent analgesic than morphine but has a shorter duration of action. The production of heroin is outlawed in the U.S. and in most other countries because of its high addiction liability. **Dihydromorphinone**, U.S.P. XIV, N.N.R. (Dilaudid, 17), is a more potent analgesic than morphine with a shorter duration of action. It was formerly widely used as an analgesic, but it is highly addicting. **Metopon**, N.N.R. (methyldihydromorphinone, 18), is also somewhat more potent than morphine, but, in contrast to heroin and dihydromorphinone, tolerance and physical dependence develop slowly. It is also less soporific than morphine. (See 81.)

Rearrangement of morphine with loss of water produces **apomorphine**, U.S.P. XIV (19), which is primarily a central nervous system stimulant. Apomorphine, as well as morphine and its other derivatives, produces emesis by a direct action on the chemoreceptor trigger zone of the medulla (18). Large doses of apomorphine may produce increased motor activity and convulsions. The dehydro dimethyl analog of morphine (**thebaine**, 20) is also a central nervous system stimulant. It has no therapeutic applications.

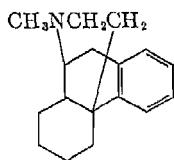


(19)

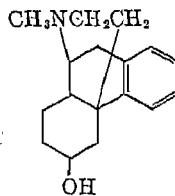


(20)

**Synthetic Narcotic Analgesics.** Most efforts to produce more potent analgesics by chemical alteration of the morphine molecule have resulted in drugs which are also more toxic and have a greater addiction liability. However, synthetic work in other series of compounds has produced agents which appear to have certain advantages over the natural or partially synthetic opium alkaloids (81). One of the closest synthetic approaches to the structure of morphine is seen in *N*-**methylmorphinan** (21).



(21)



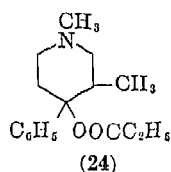
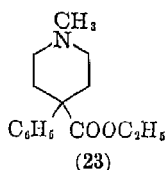
(22)

This compound lacks the ether bridge characteristic of morphine, but its analgesic activity compares favorably with that of morphine. It was previously recognized

that the phenolic hydroxyl (absent in codeine) and the alcoholic hydroxyl (absent in desomorphine) are not essential for activity. The study of *N*-methylnorphinan finally demonstrated that none of the three oxygens, including the ether bridge, is essential for analgesic activity. However, they may markedly influence potency. For example, **racemorphan**, N.N.R. (3-hydroxy-*N*-methylnorphinan, Dromoran, **22**), is considerably more potent than *N*-methylnorphinan (14). Recently racemorphan has been separated into the *levo* and *dextro* forms. The *levo* form is about twice as potent as the racemic mixture.

**Methadone**, N.N.R. (6-dimethylamino-4,4-diphenyl-3-heptanone),  $(\text{CH}_3)_2\text{NCH}(\text{CH}_3)\text{CH}_2\text{C}(\text{C}_6\text{H}_5)_2\text{COC}_2\text{H}_5$ , was synthesized in Germany during World War II. It occurs as the racemic mixture which is a more potent analgesic than morphine and produces much less smooth muscle spasm. The *levo* isomer of methadone is responsible for most of the analgesic activity of the racemic mixture. A related compound, **isomethadone** (6-dimethylamino-4,4-diphenyl-5-methyl-3-hexanone),  $(\text{CH}_3)_2\text{NCH}_2\text{CH}(\text{CH}_3)\text{C}(\text{C}_6\text{H}_5)_2\text{COC}_2\text{H}_5$ , also occurs as a racemic mixture which is somewhat less potent than methadone but has fewer side effects. Its *levo* isomer is also the more active. (See 81.)

**Meperidine**, U.S.P. XIV, N.N.R. (ethyl 1-methyl-4-phenyl-4-piperidinecarboxylate, Demerol, **23**) (see Vol. 1, p. 852), was the first of the synthetic narcotic analgesics to be of major therapeutic importance (81). It is chemically more closely related to the synthetic atropine substitutes (p. 33) than it is to morphine, and it is a much less potent analgesic than morphine. Meperidine possesses mild antispasmodic as well as analgesic activity and is frequently used as an analgesic in obstetrics because



it produces less respiratory depression than morphine. Another synthetic drug which may be used for obstetrical analgesia is **prisilidene** (1,3-dimethyl-4-phenyl-4-propionyloxypiperidine, 1,3-dimethyl-4-phenyl-4-piperidylpropionate, Nisentil, **24**). This compound has a shorter duration of action and is less potent than morphine. It appears to produce minimal respiratory depression.

*Uses of Narcotic Analgesics.* Narcotics are used primarily to relieve pain. Because they produce euphoria and physical dependence with chronic use, they present an important medicosociological problem. Morphine is widely used in therapeutics to alleviate acute pain, and meperidine, methadone, metopon, and racemorphan may be used under similar circumstances. Morphine is frequently used with atropine or scopolamine (p. 32) for preoperative medication. Here the analgesic, calming, and sedative effects are all desirable, and consequently morphine is still superior to the synthetic substitutes. The constipating properties of morphine have been used in various opium preparations to control severe diarrhea. Codeine is less potent than morphine and is used, frequently in combination with a salicylate, to control moderate pain. It is also used as an antitussive in cough preparations. Metopon is used in ambulatory patients with chronic severe pain, but it appears to be less satisfactory than racemorphan. Methadone is frequently substituted for morphine in the treat-

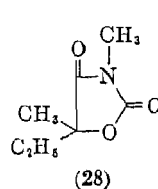
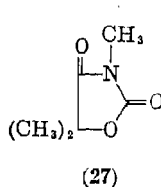
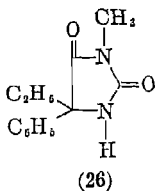
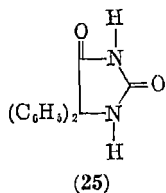
ment of drug addiction because the response to methadone withdrawal is much less severe than that to withdrawal of most other narcotics. Meperidine is the analgesic most widely used in obstetrics because it does not produce much respiratory depression. In contrast to morphine, meperidine is not spasmogenic, a factor of some importance in treating pain due to smooth muscle spasm.

#### ANTIPYRETIC ANALGESICS

A group of compounds including the **salicylates**, **cinchophen derivatives**, **aminopyrine**, U.S.P. XIV, N.F. IX, and **acetophenetidin**, U.S.P. XIV, N.F. IX, are recognized to have antipyretic and mild analgesic properties. These agents effectively lower body temperature when it is elevated but do not alter normal body temperature. Abundant clinical observations indicate that members of this group have relatively weak, but definite, analgesic activity. However, it has been impossible to confirm this action consistently in animals by the currently available testing procedures. These agents also have an anti-inflammatory action in certain diseases such as rheumatic fever and rheumatoid arthritis, but the mechanism is poorly understood. See also *Acetylsalicylic acid*; *Analgesics and antipyretics*; *Salicylic acid*.

#### ANTICONVULSANTS

Although most central nervous system depressants prevent or abort epileptic seizures if given in sufficient amounts, relatively few do so without seriously affecting the state of consciousness. **Bromide salts** (as NaBr, U.S.P. XIV), which were the first useful anticonvulsants, prevent seizures only at levels at which the patient is obviously depressed. **Phenobarbital** is definitely superior to the bromides because sedation is not severe with anticonvulsant doses (see pp. 9-10 for phenobarbital and its congeners, such as mephobarbital, with anticonvulsant properties). Since about 1935 several agents have been discovered which reduce the incidence of epileptic seizures in doses which produce little sedation. (See 84,85.) **Diphenylhydantoin**, U.S.P. XIV, N.N.R. (5,5-diphenylhydantoin, Dilantin, **25**), was the first successful nonbarbiturate anticonvulsant, although **5-phenyl-5-ethylhydantoin** (Nirvanol) was studied earlier and has some anticonvulsant properties. Diphenylhydantoin is used chiefly in the symptomatic therapy of grand mal epilepsy. **Mesantoin** (3-methyl-5-ethyl-5-phenylhydantoin, **26**) is also effective in grand mal epilepsy. It appears to cause somewhat more serious side effects than diphenylhydantoin and is used primarily in cases where the latter is ineffective. The hydantoin derivatives are of little value in patients with petit mal seizures and may occasionally produce an increase in the frequency of attacks.

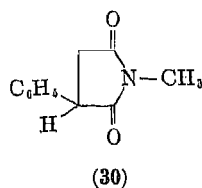
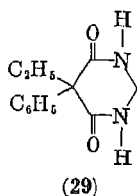


**Oxazolidine derivatives**, of which **trimethadione**, U.S.P. XIV, N.N.R. (3,5,5-trimethyl-2,4-dioxazolidine-2,4-dione, Tridione, **27**), is the best known, are useful in controlling petit mal seizures. In large doses or in sensitive patients trimethadione produces drowsiness. It occasionally causes bone marrow alterations. A derivative of

trimethadione, **paramethadione**, N.N.R. (3,5-dimethyl-5-ethyloxazolidine-2,4-dione, Paradione, 28), has similar pharmacological properties. Paramethadione occasionally is useful in cases of petit mal epilepsy in which trimethadione is ineffective.

A new compound structurally related to phenobarbital, but having two atoms of hydrogen replacing the urea oxygen of the barbituric acid nucleus, has been investigated recently. This agent, **Mysoline** (5-phenyl-5-ethylhexahydropyrimidine-4,6-dione, 29) has an anticonvulsant spectrum similar to that of diphenylhydantoin. Early clinical reports indicate that it has important undesirable side effects.

The search for new anticonvulsants has led to the development of several promising compounds which lack the heterocyclic nucleus characteristic of previously mentioned anticonvulsants. **Phenacemide**, N.N.R. (phenacetylurea, Phenurone),  $C_6H_5-CH_2CONHCONH_2$ , is one of these. The drug is effective in some cases of grand mal and petit mal, but it is used especially in the treatment of psychomotor epilepsy, a condition which is poorly controlled by other agents. Serious side effects which limit its use include damage to the bone marrow and liver and personality changes.



**Hibicon** (*N*-benzyl- $\beta$ -chloropropionamide),  $C_6H_5CH_2NHOCCH_2CH_2Cl$ , appears to have anticonvulsant properties similar to those of diphenylhydantoin, but it does not have any marked advantages over the latter compound. A related drug, **atro-lactamide** ( $\alpha$ -phenyl- $\alpha$ -hydroxypropionamide, Themisone),  $C_6H_5C(CH_3)(OH)CONH_2$ , has a wide anticonvulsant spectrum and may prove useful in the treatment of grand mal, petit mal, and psychomotor epilepsy. Its use may be limited by side effects including a toxic leukopenia.

A number of **2-phenylsuccinimides** have been reported to have anticonvulsant activity. The outstanding member of this series of compounds is **Milontin** (*N*-methyl-2-phenylsuccinimide, 30). This agent is useful in petit mal epilepsy, but it appears to be less efficacious than trimethadione. See also *Heterocyclic compounds; Hypnotics and sedatives*.

#### MISCELLANEOUS CENTRAL NERVOUS SYSTEM DEPRESSANTS

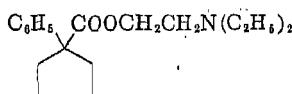
Many unrelated compounds with diverse pharmacological properties produce depression of the central nervous system. Several antihistaminics (see *Histamine and antihistamine agents*) produce such a depression. **Diphenhydramine**, U.S.P. XIV, N.N.R. (2-dimethylaminoethyl benzhydryl ether, Benadryl),  $(C_6H_5)_2CHOCH_2CH_2N(CH_3)_2$ , is usually the most effective sedative in this group, but the sensitivity of individual patients to the central nervous system depressant effects of different antihistaminics varies considerably. The antihistaminics are sometimes used to advantage for their sedative effects, particularly in children.

The central nervous system effects of several naturally occurring muscarinic blocking agents (p. 32) have been utilized for many years in the treatment of Parkinsonism, a disease characterized by rigidity and tremor of the extremities. More

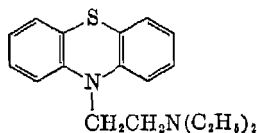


recently a group of synthetic drugs with muscarinic blocking or antihistaminic activity or both have been introduced in the treatment of this disease. It is difficult to classify these agents as stimulants or depressants of nervous activity with any accuracy because features of both depression and stimulation may be observed. They are usually more effective in reducing the rigidity than the tremor of Parkinsonism (32). Considerable variability in response is observed. One patient may receive great benefit from a particular drug, while another may be unaffected by the same agent but relieved by a different one.

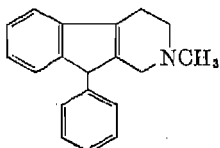
One useful synthetic agent is **trihexyphenidyl**, N.N.R. (3-(1-piperidyl)-1-cyclohexyl-1-phenyl-1-propanol, Artane),  $\text{HOC}(\text{C}_6\text{H}_5)(\text{C}_6\text{H}_{11})\text{CH}_2\text{CH}_2\text{NC}_5\text{H}_{10}$ . It produces less muscarinic blockade than atropine, while retaining some of the desired central effects of the latter. In small doses trihexyphenidyl produces depression, but in large doses excitation of the central nervous system. **Cycrimine** (3-(1-piperidyl)-1-cyclopentyl-1-phenyl-1-propanol, Pagitane, Compound 08958), which is closely related structurally to trihexyphenidyl, has been introduced recently. It has some muscarinic blocking properties and is reported to be an effective therapeutic agent (57). Another synthetic muscarinic blocking agent, **caramiphen** (2-diethylaminoethyl 1-phenylcyclopentanecarboxylate, Parpanit, Panparnit, **31**) is also used in the treatment of Parkinsonism. Although it is effective in some cases, it has many side effects which can restrict its use. **Diethazine** (10-(2-diethylaminoethyl)phenothiazine, Diparcol, **32**), which has some antihistaminic activity, appears to be less useful than atropine in



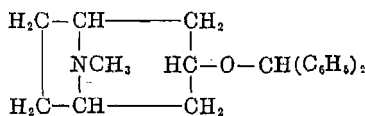
(31)



(32)



(33)



(34)

the treatment of Parkinsonism. A closely related compound **Chlorpromazine** (10-(3-dimethylaminopropyl)-2-chlorophenothiazine, Thorazine) produces depression of the central nervous system, the characteristics of which have not been adequately studied. Apparently both sensory and motor functions are altered. The drug also has some antihistaminic and adrenergic blocking activity. It has been employed in a variety of clinical conditions, but most of the reported studies have been poorly controlled and do not allow an evaluation of its clinical status. Other antihistaminic agents such as diphenhydramine and **phenindamine** (2-methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene, Thephorin, **33**) also appear to be less effective than atropine in most cases. **Benztropine** (tropine benzhydryl ether, MK-02, **34**) is related structurally to both diphenhydramine and atropine and has both antihistaminic and muscarinic blocking activity. Alone it is only slightly effective in Parkinsonism, but it appears to be useful when administered with trihexyphenidyl (**33**).

Many types of drugs produce miscellaneous central nervous system effects which can be considered depressant in general. **Reserpine** (Serpasil), an alkaloid from *Rauwolfia serpentina*, produces hypotension and sedation by a central action. Other agents produce effects which have characteristics of both stimulation and depression, such as the hallucinations produced by **mescaline**, **D-lysergic acid diethylamide** (LSD 25), and **cannabinol derivatives**. More bizarre central nervous system effects include the catatonic-like state produced by **bulbocapnine**.

### **Adrenergic Stimulants (Sympathomimetics)**

The sympathomimetics elicit responses in the body which simulate those resulting from stimulation of adrenergic nerves. This correlation is to be expected, because it is now known that adrenergic nerves produce their effects by liberating norepinephrine and, to a lesser extent, epinephrine at the nerve endings (37). These neurohormones then act upon the receptor sites of effector cells to produce characteristic adrenergic responses (Table I, p. 2). The same amines are released into the blood stream by the adrenal medulla, but the relative amounts are reversed, with epinephrine predominating in most species.

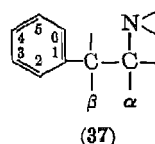
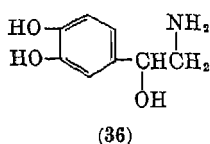
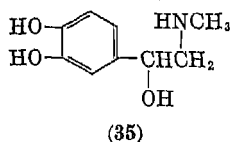
Several hundred sympathomimetic agents, both natural and synthetic, have been studied pharmacologically, and it can be said with some assurance that all true sympathomimetics produce effects which are qualitatively the same. However, quantitative variations in the magnitudes of various actions are so great that closely related agents may appear grossly to give diametrically opposite effects. The major actions of the sympathomimetic amines may be divided into five categories: (a) Excitatory actions on smooth muscle and gland cells. This category includes many of the most striking effects of the sympathomimetics, including peripheral vasoconstriction with a consequent rise in blood pressure, pupillary dilatation, secretion of salivary and some sweat glands, and the pilomotor response (producing goose flesh). (b) Inhibitory actions. These include some peripheral vasodilatation, particularly of the blood vessels supplying skeletal muscle, bronchial dilatation, and gastrointestinal relaxation. (c) Cardiac stimulation. This is evident as an increase in heart rate and in the strength of contraction, and, under certain circumstances, as abnormal cardiac rhythms. (d) Central nervous system stimulation. This is seen as stimulation of respiration, particularly in the presence of central nervous system depression, increased motor activity, and interference with normal sleep. (e) Metabolic effects. The most commonly observed metabolic effects of the sympathomimetic amines are increases in the blood glucose and lactic acid levels. Less adequately understood actions which probably fall in this category are changes in blood potassium, in electrolyte excretion by the kidney, and in overall oxygen consumption.

The sympathomimetic amines vary widely in their absolute potencies. However, the potency ratio with respect to the various properties of each amine is of greater practical importance. This is particularly apparent in relation to excitatory, inhibitory, and cardiac actions. An agent with relatively strong excitatory and cardiac stimulant actions will produce an abrupt rise in blood pressure, while a related compound with relatively greater inhibitory action may produce a fall in blood pressure, although it may have significant peripheral vasoconstrictor and cardiac stimulant actions.

The common sympathomimetic agents may be grouped as phenethylamine derivatives, aliphatic and alicyclic amines, and a small group with miscellaneous structures.

## PHENETHYLAMINES

Phenethylamine and its derivatives, including **epinephrine** (*q.v.*), U.S.P. XIV (1-(3,4-dihydroxyphenyl)-2-methylaminoethanol, Adrenalin, **35**), and **norepinephrine** (1-(3,4-dihydroxyphenyl)-2-aminoethanol, arterenol, **36**), both of which occur naturally in the more active levo form, comprise by far the largest and most thoroughly studied group of sympathomimetic agents. These compounds have been named by

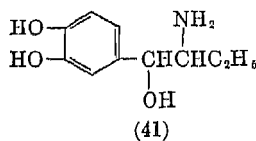
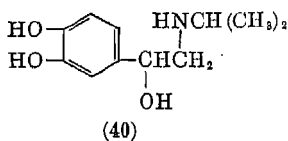
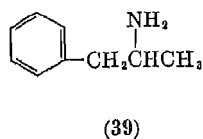
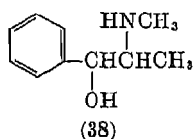


a variety of conventions, and as derivatives of various portions of the molecule. To facilitate comparisons they all will be considered here as derivatives of the  $\beta$ (or 2)-phenylethylamine (phenethylamine) nucleus (**37**). However, in some instances this procedure results in unnecessarily complicated systematic names, and simpler naming procedures will be employed with reference to specific agents.

Within the phenethylamine series, separation of the aromatic moiety and the nitrogen by two carbons produces maximal activity. Excitatory potency is enhanced by the presence of phenolic hydroxyl groups in the 3- and 4-positions (particularly the 3-position; the 2- and 5-hydroxyl substitutions are relatively ineffective), by the presence of a  $\beta$ -alcoholic hydroxyl, and by the presence of a methyl group on the nitrogen. The phenolic hydroxyls are of particular importance, and, although compounds without these groupings are capable of stimulating smooth muscle and of raising the blood pressure, such agents are usually several hundred times less active than epinephrine. Methoxyl, nitro, and amino groupings are relatively ineffective substitutes for the phenolic hydroxyl groups. The fact that the *N*-methyl group of epinephrine increases excitatory potency is frequently overlooked. In the intact animal norepinephrine may be a more effective pressor agent than epinephrine. However, this is due to the fact that pressor responses are the algebraic sum of pressor and depressor effects, and in the case of epinephrine part of the pressor effect of vasoconstriction is masked by concomitant vasodilatation. Actually, epinephrine is the more effective vasoconstrictor in most vascular beds. The *N*-methyl and  $\beta$ -alcoholic hydroxyl substituents are of limited importance except in pyrocatechol derivatives. Alkyl substituents in the  $\alpha$ -position are of relatively minor importance for excitatory potency, but agents with such substituents tend to be more stable in the body and more effective when administered orally. Compounds of this type (for example, **ephedrine**, U.S.P. XIV, N.F. IX (1-phenyl-2-methylamino-1-propanol, **38**, and **amphetamine**, U.S.P. XIV, N.N.R.,  $\alpha$ -methylphenethylamine, Benzedrine, **39**) are not deaminated by monoamine oxidase and may act as effective inhibitors of this enzyme. Although it is intriguing to speculate that these agents may produce their effects through inactivation of monoamine oxidase in a manner analogous to the action of physostigmine on cholinesterases (p. 29), it must be concluded that these amines, in common with all other sympathomimetics, act predominantly on effector cells and that enzyme inhibition plays no more than a minor role in their pharmacology. (See 2,12,16,55.)

Inhibitory activity is dependent particularly upon the presence of phenolic hydroxyl groups, *N*-alkyl, and  $\alpha$ -alkyl groupings. Although the phenolic hydroxyl

groups markedly increase excitatory potency, they are even more important in producing inhibitory effects. Consequently compounds containing phenolic hydroxyl groups, especially pyrocatechol derivatives, have higher ratios of inhibitory to excitatory activity than their nonphenolic congeners. This is particularly true if a methyl or larger alkyl group is present on the nitrogen. An *N*-alkyl substituent is very important for effective inhibitory activity. *N*-Substituents larger than methyl

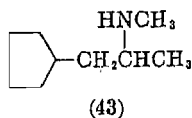
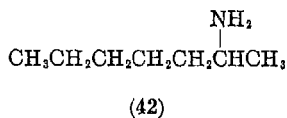


tend to produce agents with depressor activity, which is usually maximal with isopropyl or *tert*-butyl groups, as in **isopropylarterenol**, N.N.R. (1-(3,4-dihydroxyphenyl)-2-isopropylaminoethanol, Isuprel, 40). However, the appearance of this depressor response is dependent more upon a reduction in excitatory than upon an absolute increase in inhibitory activity. The presence of a  $\beta$ -alcoholic hydroxyl increases essentially equally excitatory and inhibitory activity and therefore does not change the nature of the response. Inhibitory activity is also increased by alkyl substituents on the  $\alpha$ -carbon. The substitution of a 2-carbon chain in this position of norepinephrine produces **ethylnorepinephrine** (1-(3,4-dihydroxyphenyl)-2-amino-1-butanol, Butanefrine, 41), a compound with limited pressor activity but with a strong bronchodilator action. The relation of chemical structure to inhibitory activity depends somewhat on the test object; in particular, intestinal relaxation varies considerably from other responses. (See 2,9,12,55,63.)

The structural requirements for cardiac activity among the phenethylamines are difficult to assess precisely. Compounds with either a potent excitatory or a potent inhibitory action tend to have strong cardiac effects. However, in general, the cardiac action follows more closely the inhibitory than the excitatory activity. Stimulation of the central nervous system by the sympathomimetic amines is largely dependent upon the presence of an aromatic ring. Both phenolic and nonphenolic compounds possess this action. However, from a practical standpoint, all the compounds which are employed clinically for their central excitant effects (ephedrine (38), amphetamine (39), methamphetamine, etc.) are without phenolic hydroxyl substituents. The reason for this is not that the hydroxyl groups reduce central stimulant activity, but that they so increase the pressor and cardiac stimulant actions that doses of the hydroxylated compounds sufficiently large to produce useful stimulation of the central nervous system cannot be administered safely. Metabolic activity among phenethylamines appears to be favored by the presence of phenolic hydroxyl groups and an *N*-alkyl grouping. However, details of the relation of chemical structure to this activity have been inadequately studied.

## ALIPHATIC AND ALICYCLIC AMINES

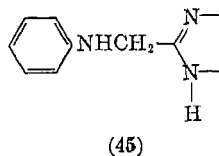
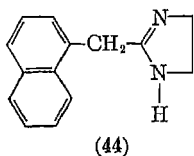
Straight-chain compounds such as **tuaminoheptane**, N.N.R. (2-aminoheptane, Tuamine, 42), and agents which include a saturated ring structure such as **cyclopentamine**, N.N.R. (1-cyclopentyl-2-methylaminopropane, Clonane, 43), possess similar pharmacological properties. Sympathomimetic activity appears in compounds with a minimum of 4 carbon atoms and is usually maximal with 6 or 7. In general,



the aliphatic and alicyclic amines possess weak central nervous stimulant and inhibitory actions and reasonably potent excitatory and cardiac actions. All the members of this group are much less potent than compounds such as epinephrine and norepinephrine. In this series *N*-methyl substitution does not increase excitatory and inhibitory activity as in the phenethylamines. (See 2,12,80.)

## MISCELLANEOUS ADRENERGIC STIMULANTS

Although many types of compounds in addition to those discussed above possess certain actions which may be termed "sympathomimetic" (1), the only agents in this category with sympathomimetic effects of practical importance are certain **imidazoline derivatives**. Several of these, including **naphazoline**, U.S.P. XIV, N.N.R. (2-(1-



naphthylmethyl)-2-imidazoline, Privine, 44), and **Otrivine** (2-anilinomethyl-2-imidazoline, 45) possess pressor activity essentially equal to that of epinephrine. These compounds are also effective cardiac stimulants but possess only weak inhibitory and central stimulant activities. (See 67.)

## USES OF ADRENERGIC STIMULANTS

Clinical exploitation of excitatory actions of the sympathomimetics is largely limited to the production of vasoconstriction, either locally or systemically. Several of the local uses, such as to reduce the absorption and prolong the action of local anesthetics and to reduce the engorgement of the nasal mucosa in rhinitis, are well established. However, a secondary dilatation following prolonged use of these agents as nasal decongestants may be troublesome. The sympathomimetics are used to raise the blood pressure in a variety of hypotensive conditions, although the benefit to the patient in many of these situations is questionable. Their value in shock is highly debatable because they tend to increase blood pressure at the expense of blood flow. Some sympathomimetics may be used to produce mydriasis without cycloplegia. The inhibitory actions of the sympathomimetics are used to advantage in relieving the bronchospasm associated with asthma. Both excitatory and inhibitory effects may be involved in the favorable response to epinephrine and related amines when administered in a variety of acute allergic conditions. The cardiac stimulant action

is occasionally of value in cases of complete heart block. Although epinephrine is frequently administered by the intracardiac route after cessation of heart action, it is doubtful if many lives have been saved by this procedure. Central nervous system actions of the sympathomimetics are widely employed in conditions of mental depression and to control the appetite. Amphetamine and methamphetamine are useful analeptics to combat poisoning from many central nervous system depressants. Their central stimulant action is effective and prolonged, and it involves little of the danger of convulsions from overdosage which is associated with many central stimulants (p. 3). Metabolic effects of the sympathomimetics are of little clinical importance, although epinephrine is occasionally employed to raise the level of blood glucose in hypoglycemic crises.

### Adrenergic Blocking Agents

The term adrenergic blocking agents designates compounds which selectively inhibit responses of effector cells to adrenergic sympathetic nerve impulses and to epinephrine and other sympathomimetics. It is to be emphasized that the action of agents of this type is not upon sympathetic nerve endings nor upon the adrenergic mediators, as might be implied by the less accurate terms sympatholytic and adrenolytic agents. The distinction between adrenolytic and sympatholytic properties is largely artificial. Although some agents inhibit responses to circulating sympathomimetics much more effectively than responses to sympathetic nerve impulses, the difference is only quantitative; all known adrenergic blocking agents are more effective against responses to circulating mediators than against responses to sympathetic nerve activity.

The fact that responses to adrenergic stimuli can be blocked or reversed by drugs has been known for fifty years. However, until a few years ago adrenergic blocking agents were largely laboratory curiosities or investigative tools. The recent discovery of new classes of chemicals possessing potent adrenergic blocking activity has changed the picture entirely, and the experimental and clinical literature on adrenergic blockade is expanding rapidly.

Although members of the various groups of adrenergic blocking agents vary widely in potency, in effectiveness, and in type and importance of side reactions, certain qualitative generalizations can be made (1,60). All adrenergic blocking agents are more effective against responses to circulating adrenergic mediators than against responses to direct sympathetic nerve activity. The basis for this difference is not understood, but it is probably not due to inhibition of penetration of the effector cells by the circulating sympathomimetics (60). All adrenergic blocking agents inhibit excitatory responses of smooth muscle and gland cells. Inhibitory responses of smooth muscle are not specifically blocked. It is true that the relaxing effect of epinephrine on some structures may be abolished, but this action has been demonstrated only in anatomically complex organs and with agents which have many actions in addition to producing adrenergic blockade. It probably involves alteration of the complex interaction of intramural nervous and smooth muscle tissues rather than a specific inhibition of the actions of epinephrine upon the smooth muscle cells themselves. Physiological responses of the mammalian heart to adrenergic stimuli (increase in rate and in strength of contraction) are also resistant to blockade, although many of the adrenergic blocking agents are effective in preventing pathological responses of the heart, such as ar-

rhythmias. Some types of blocking agents also effectively inhibit adrenergically induced hyperglycemia, but not the associated lactic acidemia. However, this effect is not well correlated with other adrenergic blocking activity, and it probably represents a pharmacological property quite different from that involved in the blockade of smooth muscle responses (43). Adrenergic blocking activity does not appear to be correlated with chemical similarity to the phenethylamine structure characteristic of most sympathomimetics.

#### $\beta$ -HALOALKYLAMINES

The  $\beta$ (or 2)-haloalkylamine series is one of the most recently discovered classes of adrenergic blocking agents. Members of this series possess outstanding characteristics of specificity, effectiveness, and prolonged action. Since the discovery of the adrenergic blocking activity of Dibenamine,  $(\text{C}_6\text{H}_5\text{CH}_2)_2\text{NCH}_2\text{CH}_2\text{Cl}$ , in 1945, over 500 congeners have been synthesized and tested pharmacologically. Although many details of the structure-activity relationship are not yet understood, certain structural requirements for Dibenamine-like activity have been established (60,61,62). (a) The compound must be a tertiary alkylamine. (b) It must have a halogen (other than fluorine) or sulfonic acid radical in the  $\beta$ -position of the alkyl group. (c) It must include at least one aromatic ring substituent in proper relation to the nitrogen to satisfy both steric and resonance requirements. The  $\beta$ -haloalkylamines do not produce blockade directly but first must form an internal ethylenimonium structure with displacement of the halide or sulfonate ion. (The rate of cyclization is sulfonic acid > bromine > chlorine.) This reactive imonium intermediate then acts as an alkylating agent, reacting most readily with sulfhydryl (mercapto) groups, and also with amino and carboxyl groups. The stability of this bonding to tissue probably accounts for both the effectiveness of the blockade produced and the prolonged action of these agents.

**Dibenamine** (*N,N*-dibenzyl-2-chloroethylamine),  $(\text{C}_6\text{H}_5\text{CH}_2)_2\text{NCH}_2\text{CH}_2\text{Cl}$ , and **phenoxybenzamine** (*N*-benzyl-*N*-(2-phenoxyisopropyl)-2-chloroethylamine, Dibenamine),  $\text{C}_6\text{H}_5\text{OCH}_2\text{CH}(\text{CH}_3)\text{N}(\text{CH}_2\text{C}_6\text{H}_5)\text{CH}_2\text{CH}_2\text{Cl}$ , are the best-known members of the  $\beta$ -haloalkylamine group of adrenergic blocking agents. Their actions are qualitatively similar, but phenoxybenzamine is 6 to 8 times more potent than Dibenamine. In addition, it is more effectively absorbed after oral administration and possesses significant antihistaminic activity. Both agents produce a blockade which develops slowly, is effective against very large doses of epinephrine and massive discharge of sympathetic nerves, and persists for several days after a single administration (60). Pressor responses to exogenous and endogenous epinephrine and to sympathetic nerve activity are reversed. This reversal results from the fact that excitatory vasoconstrictor activity is inhibited while inhibitory vasodilator activity is still expressed. Excitatory responses to other sympathomimetic agents are essentially equally blocked, but reversal depends upon the extent to which these agents exert inhibitory effects (p. 18) (63). Tachycardia is usually produced, not because of a direct action of the drugs, but because compensatory sympathetic cardiac stimulation is not blocked. Excitatory responses of other smooth muscle are blocked as readily as those of the vascular system. Side effects include central nervous system stimulation when large doses are administered rapidly intravenously, and local irritation and tissue damage following subcutaneous, intramuscular, or intraperitoneal injection (60).

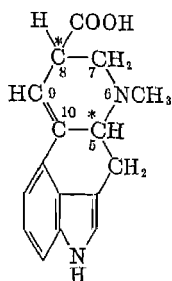
## ERGOT ALKALOIDS

The ergot alkaloids (see Vol. 1, p. 497) were the first agents demonstrated to have adrenergic blocking activity. They are produced by fungi of the genus *Claviceps* and closely related genera which are parasitic on various grains and grasses. The naturally occurring alkaloids may be divided into three groups, and L- and D-isomers of each alkaloid are known. The active L-isomers of the natural alkaloids are listed in Table VI. The D-forms contain isolysergic instead of lysergic acid (46) and are

TABLE VI. Pharmacologically Active Natural Ergot Alkaloids.

Alkaloid	Formula	Component Parts			
Ergotamine group		Lysergic acid	NH <sub>3</sub>	Pyruvic acid	L-Phenylalanine L-Leucine
Ergotamine	C <sub>33</sub> H <sub>35</sub> N <sub>5</sub> O <sub>5</sub>				
Ergosine	C <sub>30</sub> H <sub>37</sub> N <sub>5</sub> O <sub>5</sub>		D-Proline	Dimethylpyruvic acid	L-Valine L-Phenylalanine L-Leucine
Ergotoxine group					
Ergocornine	C <sub>35</sub> H <sub>39</sub> N <sub>5</sub> O <sub>5</sub>				
Ergocristine	C <sub>32</sub> H <sub>41</sub> N <sub>5</sub> O <sub>5</sub>				
Ergokryptine	C <sub>31</sub> H <sub>39</sub> N <sub>5</sub> O <sub>5</sub>				
Ergonovine	C <sub>19</sub> H <sub>23</sub> N <sub>3</sub> O <sub>2</sub>	D-2-Aminopropanol			

designated by the ending -inine (ergotamine vs. ergotaminine). They have little pharmacological activity. Only alkaloids with a peptide side chain exhibit adrenergic blocking activity. Among these, members of the ergotoxine group, which contain dimethylpyruvic acid instead of pyruvic acid as in the ergotamine group, are the more potent. Dihydro derivatives of the naturally occurring peptide alkaloids have been prepared and have been found to be uniformly more potent adrenergic blocking agents than the parent compounds, but less effective as direct smooth muscle stimulants. (See 73,78,79.)



Carbon 8, point of lysergic-isolysergic acid isomerism

Double bond at 9,10 hydrogenated in forming dihydro alkaloids

(46)

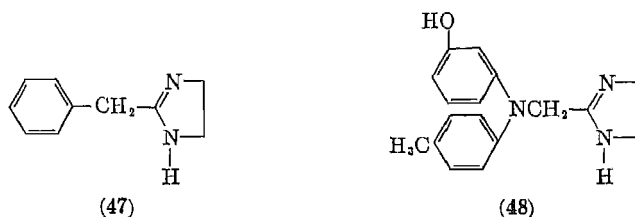
In animals all the peptide ergot alkaloids are effective in blocking excitatory responses to sympathetic nerve activity and to circulating sympathomimetic agents. Indeed, some of the hydrogenated members of the ergotoxine group are the most potent known adrenergic blocking agents (73). However, side effects, particularly a strong emetic action, seriously limit the dosage which may be administered, and significant adrenergic blockade can rarely be produced in man by tolerated doses, although peripheral vasoconstrictor tone may be reduced as a result of actions on the central nervous system (44). The most important side effects of the ergot alkaloids are direct stimulation of smooth muscle, irrespective of its innervation, and complex



excitant and depressant effects on the central nervous system. The natural alkaloids uniformly produce a rise in blood pressure. The fall in blood pressure induced in some hypertensives by the dihydrogenated alkaloids, and the slowing of heart rate and the emesis produced by all ergot alkaloids are due to effects on the central nervous system which occur with doses smaller than those required to produce significant adrenergic blockade (60).

#### IMIDAZOLINES

A large number of 2-substituted imidazolines have been synthesized, but only two have received extensive evaluation as adrenergic blocking agents. These are **benzazoline** (2-benzyl-2-imidazoline, Priscoline, 47) and **phentolamine**, N.N.R. (2-(*N*-*p*-tolyl-*N*-(*m*-hydroxyphenyl)aminomethyl)-2-imidazoline, Regitine, C-7337, 48). Minor

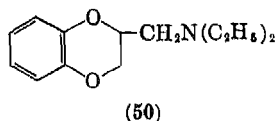
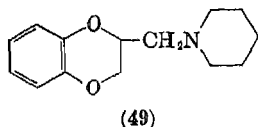


changes in the structure of these compounds produce agents with predominantly anti-histaminic (**antazoline**, N.N.R. (2-(*N*-benzylanilinomethyl)-2-imidazoline, Antistine) or sympathomimetic (**naphazoline**, U.S.P. XIV, N.N.R. (2-(1-naphthylmethyl)-2-imidazoline, Privine, 44) actions. Benzazoline and phentolamine are moderately effective adrenergic blocking agents. In tolerated doses in man they produce a greater blockade than can be obtained with the ergot alkaloids but a less complete blockade than that afforded by the  $\beta$ -haloalkylamines. Their blocking action is relatively transient. These agents also exhibit important direct actions upon cardiac and smooth muscle, many of which are produced by doses smaller than those required to evoke even minimal adrenergic blockade. In general, side effects of the imidazoline adrenergic blocking agents can be divided into three classes: (a) sympathomimetic, including cardiac stimulation and coronary artery dilatation; (b) parasympathomimetic, including marked stimulation of gastrointestinal motility, and (c) histamine-like, including stimulation of gastric secretion, peripheral vasodilatation, and a pressor effect in rabbits. The most distressing side effects in patients are cardiac and gastrointestinal tract stimulation. Phentolamine is a more potent adrenergic blocking agent than benzazoline, and its side effects are somewhat less prominent. Benzazoline and phentolamine may cause peripheral vasodilatation and a fall in blood pressure due to both direct peripheral dilatation and adrenergic blockade. However, the fall in blood pressure may be minimal or absent because of the antagonistic effect of cardiac stimulation. (See 10,41,60,71.)

#### BENZODIOXANS

The benzodioxans were the first synthetic adrenergic blocking agents of importance. They are moderately effective in inhibiting excitatory responses of smooth muscle to adrenergic stimuli, but the blockade produced is relatively transient and the clinical and experimental usefulness of these agents is considerably limited by their many important side effects. Some members of the group (for example, **piperoxan**,

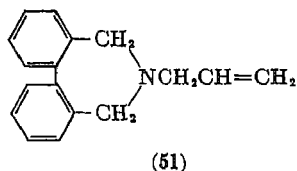
N.N.R. 2-(1-piperidylmethyl)-1,4-benzodioxan, Benodaine, 933F, **49**) are effective mainly against responses to circulating sympathomimetic agents, whereas others (for example, **Prosympal**, 2-(diethylaminomethyl)-1,4-benzodioxan, 883F, **50**) also have



considerable activity against responses to sympathetic nerve impulses. Important side effects of the benzodioxans include direct stimulation of many different smooth muscle structures, direct depression of the myocardium, and mixed central nervous system stimulation and depression leading to increased vagal and sympathetic tone, and depression of cardiovascular reflexes. The combination of direct smooth muscle stimulation and centrally induced sympathetic activity leads to an increase in blood pressure in unanesthetized animals and man. (See 1,60.)

#### MISCELLANEOUS ADRENERGIC BLOCKING AGENTS

In addition to the groups discussed above, many other types of compounds have been demonstrated to possess adrenergic blocking activity. These include **dibenzazepine derivatives** (6-allyl-6,7-dihydro-5H-dibenz[*c,e*]azepine, **Ilidar**, Ro 2-3248, **51**) (70), primary and secondary **2-phenoxyethylamines**, particularly when substituted in the 1-position, **tetrahydroisoquinolines**, **phenylethylenediamines**, **phenylhydrazines**,



several **sympathomimetics**, **yohimbine** and its congeners and derivatives, **cinchona** and **alstonia alkaloids**, **bulbocapnine**, **boldine**, and extracts of *Galium aparine* and *Rauwolfia*. (See also *Alkaloids*.) Most of these agents have relatively weak adrenergic blocking activity and have been largely neglected in recent years in favor of intensive investigation of members of the first three series of compounds mentioned above. (See also 1,60.)

#### USES OF ADRENERGIC BLOCKING AGENTS

Phenoxybenzamine is now undergoing extensive clinical trial in the treatment of hypertension, pheochromocytoma, peripheral vascular disease, glaucoma, cardio-spasm, and cardiac arrhythmias (40). Because of its recent introduction into medicine and the lack of previous experience with effective adrenergic blocking agents, its role in clinical medicine is still to be established. However, it appears to produce a more complete blockade of peripheral sympathetic tone than any other available adrenergic blocking agent. Dibenamine and phenoxybenzamine also appear to be effective in preventing the development of irreversible shock in animals, and a cautious trial of these agents in clinical shock seems to be indicated. Their specificity of action allows them to be used experimentally to distinguish between adrenergic and nonadrenergic stimuli.

The naturally occurring ergot alkaloids, particularly ergonovine and related partially synthetic compounds, and ergotamine, are widely used as oxytocics and in the treatment of migraine because of their direct smooth muscle stimulant action. The dihydrogenated members of the ergotoxine complex have been tried in the treatment of hypertension and peripheral vascular disease. The moderate fall in blood pressure and the peripheral vasodilatation produced by parenteral administration of these agents are due to effects on the central nervous system rather than to adrenergic blockade. The beneficial effects obtained have usually been limited, and, in general, the ergot alkaloids appear to be inferior to several other types of adrenergic blocking agents for reducing peripheral vascular tone (40).

Both benzazoline and phentolamine have been employed with moderate success as vasodilators in peripheral vascular disease (40,71). In addition, small doses of phentolamine administered intravenously may be employed as a test for hypertension due to functional tumors of the adrenal medulla or other chromaffin tissue.

The only clinical application of the benzodioxans (piperoxan) is in diagnosis of hormone-producing tumors of the adrenal medulla and other chromaffin tissue (pheochromocytoma). In the presence of hypertension induced by circulating adrenergic agents, piperoxan causes a fall in blood pressure, while in cases of essential hypertension the pressure rises. Unpleasant and alarming side effects are not uncommonly observed during the administration of piperoxan.

### Cholinergic Stimulants (Parasympathomimetics)

The term parasympathomimetic is applied to drugs which elicit responses similar to those resulting from activity of the parasympathetic nervous system. However, it should be remembered that many such agents also mimic the effects of other divisions of the nervous system. Although not the first such drug studied, acetylcholine is the type compound of this group. Just as excitation of the sympathetic nervous system causes the release of an epinephrine- or norepinephrine-like substance, excitation of the parasympathetic nervous system causes the release of an acetylcholine-like substance at the postganglionic nerve endings. Much evidence has accumulated to support the hypothesis that this neurohormone is indeed acetylcholine (56,72). Characteristic cholinergic responses (Table I, p. 2) are produced by the direct action of the released acetylcholine upon the receptor sites of effector cells. It is now generally accepted that acetylcholine is involved in the mediation of nerve effects at parasympathetic and some sympathetic postganglionic junctions with cardiac and smooth muscle and gland cells, at autonomic ganglia, and at the skeletal neuromuscular junction. The responses are terminated by hydrolysis of the mediator by cholinesterases. Specific or true acetylcholinesterases are present in high concentration in the vicinity of cholinergic nerve endings, and diverse nonspecific esterases capable of hydrolyzing acetylcholine (pseudocholinesterases) are present in plasma and in many other tissues. The effects of injected acetylcholine or of cholinergic nerve stimulation may be enhanced and prolonged by prior administration of cholinesterase inhibitors.

The actions of acetylcholine on autonomic ganglia and on the skeletal neuromuscular junction are referred to as *nicotinic* because they are similar to those of nicotine; that is, small doses stimulate and facilitate transmission, while large doses depress transmission. The actions of acetylcholine on peripheral autonomic effector cells, such as smooth muscle, are referred to as *muscarinic* because they are similar to

those of the alkaloid muscarine. The effects of acetylcholine have been related to those of nicotine and muscarine because the pharmacology of these alkaloids was thoroughly studied long before acetylcholine attracted attention (27). Muscarinic responses are usually elicited by smaller amounts of acetylcholine than are nicotinic responses and frequently mask the latter. However, after administration of muscarinic blocking agents (p. 32) the nicotinic actions of acetylcholine are readily demonstrated.

Drugs which mimic the effects of stimulation of cholinergic nerves may be divided into three main categories: choline derivatives, anticholinesterases, and miscellaneous cholinergic stimulants.

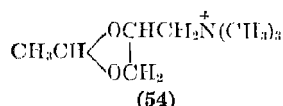
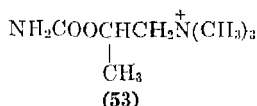
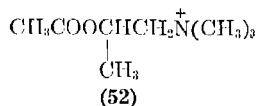
#### CHOLINE DERIVATIVES

Most choline derivatives reproduce some of the effects of cholinergic nerve stimulation. (See also *Cardiovascular agents*.) However, they differ considerably in the relative potencies of their muscarinic and nicotinic actions as well as in their susceptibility to hydrolysis by cholinesterases. **Choline** (*q.v.*), N.N.R. ((2-hydroxyethyl)trimethylammonium),  $\text{HOCH}_2\text{CH}_2\text{N}^+(\text{CH}_3)_3$ , is widely distributed in living matter as a constituent of phospholipides. In large doses it produces characteristic cholinergic effects. A cationic charge appears to be important for cholinergic activity, and many onium compounds (*q.v.*), including sulfonium, phosphonium, stibonium, and arsonium, possess cholinergic properties (46). Stimulant activity is exerted particularly by compounds with three or more methyl substituents. Substitution of the alcoholic hydroxyl group of choline produces agents with much greater pharmacological activity (11). **Acetylcholine** ((2-acetoxyethyl)trimethylammonium),  $\text{CH}_3\text{COOCH}_2\text{CH}_2\text{N}^+(\text{CH}_3)_3$  (see Vol. 3, p. 924), for example, is several thousand times more potent than choline. Maximal cholinergic stimulant activity appears to require an adequate cationic charge, as in choline, a two-carbon alkyl side chain and  $-\text{CO}-$  and  $-\text{O}-$  located approximately 7 Å. and 5 Å. respectively from a methyl-substituted quaternary nitrogen (47,68). Most, but not all, potent parasympathomimetics fulfill these criteria.

The **reversed carboxyl analog of acetylcholine** ((2-carboxyethyl)trimethylammonium, methyl ester),  $\text{CH}_3\text{OOCCH}_2\text{CH}_2\text{N}^+(\text{CH}_3)_3$ , has many of the properties of acetylcholine (76). **Carbachol**, U.S.P. XIV (carbamylcholine, (2-carbamoyloxyethyl)trimethylammonium, Doryl),  $\text{NH}_2\text{COOCH}_2\text{CH}_2\text{N}^+(\text{CH}_3)_3$ , has the terminal methyl of acetylcholine replaced by an amino group. This compound has muscarinic and nicotinic properties similar to those of acetylcholine. However, it is not hydrolyzed by cholinesterases and therefore produces in the intact animal more powerful and prolonged effects than acetylcholine does. In addition to its direct cholinergic effects, carbachol is a moderately effective inhibitor of cholinesterases, and its di-*n*-butyl ethyl derivative (**Dibutoline** (2-di-*n*-butylcarbamoyloxyethyl)ethyltrimethylammonium) acts both as an anticholinesterase and as a parasympathetic and ganglionic blocking agent. Presumably its structure is sufficiently similar to that of acetylcholine to combine with enzyme and effector cell receptors, but sufficiently different that it does not produce stimulation and is not readily split by cholinesterases. Increasing the size of the ester substituent increases nicotinic activity. **Propionylcholine**, which occurs in the animal body, has a predominance of nicotinic over muscarinic effects, and **butyryl-** and **benzoylcholine** have largely nicotinic properties.

**Methacholine**, U.S.P. XIV, N.N.R. (acetyl- $\beta$ -methylcholine, Mecholyl. 52), and

its less potent congener, *O*-ethyl- $\beta$ -methylcholine, have potent muscarinic but very weak nicotinic activities. Methacholine is less rapidly hydrolyzed by cholinesterases than acetylcholine, but its actions are nevertheless quite brief. In **bethanechol**, N.N.R. ((2-carbamoyloxy-2-methylethyl)trimethylammonium, Urecholine, **53**), the terminal  $\text{NH}_2$  prevents hydrolysis by cholinesterases but does not alter significantly the predominantly muscarinic effects of methacholine. The **cyclic acetal of 2,3-dihydroxypropyltrimethylammonium** (F2268, **54**) is very similar to methacholine in structure and in muscarinic activity but also possesses nicotinic properties.

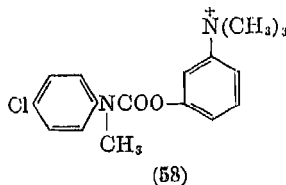
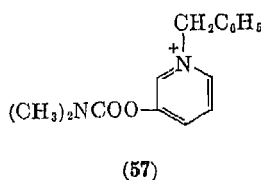
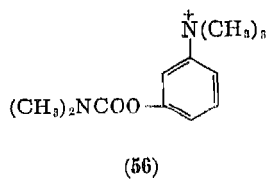
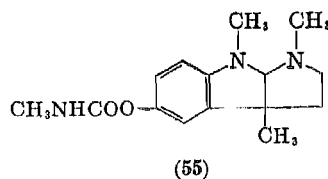


Alkyl **ether derivatives** of choline have primarily muscarinic properties, but certain aromatic ethers such as cresoxycholines (toloxycholines) have important and specific nicotinic actions. The ethyl ether of choline is a more potent muscarinic agent than are the methyl or *n*-propyl derivatives. The stimulant actions of alkyl ether derivatives of choline are primarily muscarinic, but those of **keto derivatives** are primarily nicotinic. Among keto derivatives of amyltrimethylammonium the order of nicotinic potency is 4-keto > 3-keto > 2-keto. (See 48.)

#### ANTICHOLINESTERASES

As mentioned above, cholinesterase is a generic term referring to a family of both specific (acetylcholinesterases) and nonspecific cholinesterases (87). Specific cholinesterases hydrolyze acetylcholine and methacholine, but not benzoylcholine, tributyrin, or methyl butyrate. On the other hand, most nonspecific cholinesterases hydrolyze benzoylcholine, tributyrin, and methyl butyrate, as well as acetylcholine, but not methacholine. Unlike nonspecific cholinesterases, specific cholinesterases exhibit maximal activity toward low concentrations of acetylcholine and are inhibited by an excess of substrate. The common anticholinesterases inhibit both specific and nonspecific cholinesterases, but the latter are usually more readily inhibited (52). Manifestations of cholinergic stimulation appear only when specific cholinesterase is inhibited. The anticholinesterases may produce all the responses characteristic of acetylcholine because they act by preserving this mediator. The order of appearance of organ responses to anticholinesterases is the same as for acetylcholine; muscarinic responses appear earlier and with smaller doses than nicotinic responses. In spite of therapeutic claims, there is little convincing evidence that any of these agents is significantly selective for individual organs such as the bladder or gastrointestinal tract. The brain, however, is an exception, and those anticholinesterases with the greatest lipid solubility have the greatest effect on the central nervous system and may be potent convulsant agents. Anticholinesterases may combine with the enzymes in a reversible or irreversible manner.

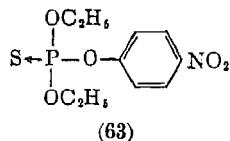
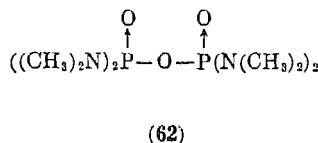
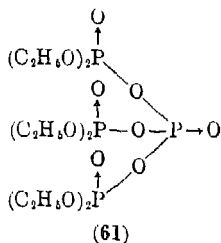
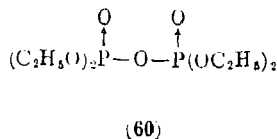
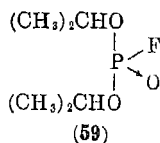
**Reversible Anticholinesterases.** The classical example of a reversible anticholinesterase is **physostigmine**, U.S.P. XIV (methylcarbamate of eseroline, eserine, **55**) (see Vol. 1, p. 499), an alkaloid obtained from the calabar bean. On standing in solution, it is readily decomposed to eseroline, which is pharmacologically inactive, and then to rubresceine which has  $\frac{1}{100}$  the anticholinesterase activity of physostigmine (36). Physostigmine combines with cholinesterase throughout the body and therefore



produces diffuse cholinergic effects including increased intestinal peristalsis, miosis, increased salivation, skeletal muscle fasciculation, and, in large doses, convulsions. A number of more stable substitutes for physostigmine have been synthesized. One of these, **neostigmine**, U.S.P. XIV, N.N.R. (*N*-(*m*-hydroxyphenyl)trimethylammonium, dimethylcarbamate, Prostigmin, **56**), effectively facilitates transmission across the neuromuscular junction both as a result of cholinesterase inhibition and by a direct action on the skeletal muscle endplates. It also produces less central nervous system excitation than physostigmine because of its lower lipid solubility. Another synthetic agent with the same pharmacological actions as neostigmine is **benzpyrinium**, N.N.R. (1-benzyl-3-(dimethylcarbamoyloxy)pyridinium, Stigmonene, **57**). The properties of the *N*-(*p*-chlorophenyl)-*N*-methylcarbamate of (*m*-hydroxyphenyl)trimethylammonium (NU 1250, **58**) are also similar to those of neostigmine. Several (3-hydroxyphenyl)trialkylammonium derivatives, of which **Edrophonium**, N.N.R. ((3-hydroxyphenyl)ethyltrimethylammonium, Tensilon) is representative, produce some inhibition of cholinesterase. However, they antagonize the skeletal muscle paralysis produced by curare more effectively than would be expected from their anticholinesterase potency, indicating a major direct effect on skeletal muscle.

**Irreversible Anticholinesterases.** In contrast to the reversible anticholinesterases, a group of organic phosphate derivatives, developed empirically during World War II as chemical warfare agents, combine with cholinesterases to form an inactive complex which is only slightly dissociable (**52**). After administration of these agents, normal cholinergic function is not restored until the enzyme reserve is regenerated, which may require several weeks for completion. **Diisopropyl fluorophosphate** (DFP, Floropryl, **59**) was the first of the irreversible anticholinesterases to receive thorough pharmacological study. Although sodium fluorophosphate inhibits cholinesterases, alkyl substituents greatly enhance activity. Three-carbon substituents, as in DFP, appear to be optimal for anticholinesterase activity. DFP preferentially combines with nonspecific cholinesterases, and a dose of DFP which completely inactivates plasma nonspecific cholinesterases may produce no visible cholinergic effects. However, adequate doses of DFP also inhibit specific cholinesterases and produce the classical signs and symptoms of cholinergic stimulation. **Tetraethyl pyrophosphate** (TEPP, **60**), **hexaethyl tetraphosphate** (HETP, probable formula, **61**), **octamethylpyrophosphoramidate** (OMPA, **62**), and **parathione** (*O,O*-diethyl *O-p*-nitrophenyl thiophosphate, **63**) have actions similar to those of DFP. However, the inactivation of cholinesterases by these agents is partially reversible, and recovery occurs much more

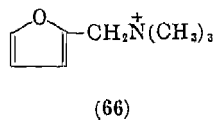
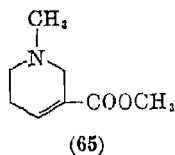
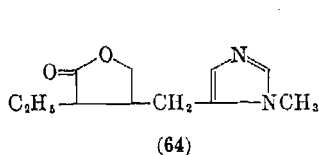
rapidly than after DFP administration. Both OMPA and parathione are converted to more active compounds *in vivo*. Members of this group of agents have less selectivity for nonspecific cholinesterases than DFP does. They also have less effect on the central nervous system because of their lower lipid solubility. See also Vol. 7, pp. 137, 896; Vol. 10, p. 507.



#### MISCELLANEOUS CHOLINERGIC STIMULANTS

Several alkaloids possess parasympathomimetic properties (1). **Muscarine**,  $\text{C}_8\text{H}_{19}\text{NO}_3$  (probably (1-ethyl-2-formyl-2-hydroxy)ethyltrimethylammonium,  $\text{OHC-CH(OH)CH(C}_2\text{H}_5\text{)N}^+(\text{CH}_3)_3$ ), obtained from the poisonous mushroom *Amanita muscaria*, is of historical interest. Responses to muscarine resemble closely those to postganglionic cholinergic nerve stimulation, and consequently such responses are referred to as muscarinic (p. 27).

**Pilocarpine**, U.S.P. XIV (64), an alkaloid obtained from a South American plant, *Pilocarpus jaborandi*, also produces characteristic muscarinic effects, but increased lacrimal, salivary, sweat, and intestinal gland secretion is particularly prominent. **Arecoline**, N.F. IX (methyl 1,2,5,6-tetrahydro-1-methylnicotinate, 65), the alkaloid of *Areca catechu* or betel nut, has pharmacological actions similar to those of pilocarpine, although its chemical structure is very different. Neither of these alkaloids is chemically related to the choline derivatives. A number of synthetic substances with



cholinergic stimulant properties are known (1). The most thoroughly studied are furfuryl derivatives containing a quaternary nitrogen. These have primarily muscarinic actions. (5-Methylfurfuryl)trimethylammonium is considerably more active than its lower homolog, **furfurethonium**, N.N.R. (furfuryltrimethylammonium, Furfmethide, 66), although the latter is the only member of this group which is employed clinically.

## USES OF CHOLINERGIC STIMULANTS

Cholinergic stimulants are of importance in only a limited number of clinical situations. The duration of action of compounds which are readily hydrolyzed by cholinesterases is too brief to be of practical value. Drugs such as methacholine, bethanechol, and furtrethonium are used occasionally in the treatment of peripheral vascular disease, urinary retention, ileus, and paroxysmal supraventricular tachycardia. They are usually administered parenterally but can be given orally. Carbamates such as bethanechol and carbachol are especially suited for oral administration. Carbachol and furtrethonium are applied locally to the eye to produce miosis.

The anticholinesterases, especially those which act reversibly, are used more frequently in therapeutics than the direct stimulants. Physostigmine is seldom administered systemically, but it is used locally in ophthalmology to produce miosis, as is DFP. Agents such as neostigmine and benzpyrinium may be given systemically to relieve bladder or bowel atony, as well as to facilitate skeletal neuromuscular transmission after curarization and in the disease myasthenia gravis. The irreversible anticholinesterases, especially TEPP, HETP, and more recently OMPA, also have been used in myasthenia gravis. Their effect is more prolonged than that of neostigmine, but the maximum muscle strength attained is less, probably because they lack a direct action on the skeletal muscle endplates. Parathione and several other anticholinesterases are used as insecticides.

Pilocarpine is used in ophthalmology to produce miosis and occasionally is given systemically to produce diaphoresis. Arecoline is used in veterinary medicine as a purge and teniaicide. Muscarine is of no clinical importance except as a toxic agent in poisoning by *Amanita muscaria*.

## Muscarinic Blocking Agents

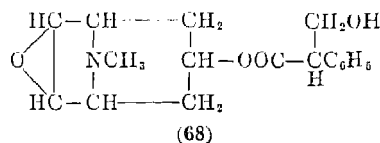
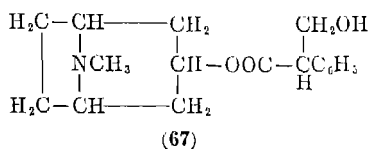
Drugs that inhibit responses of effector cells to postganglionic cholinergic nerve stimulation and to circulating cholinergic agents, that is, muscarinic responses, may be classified as muscarinic blocking agents. These drugs do not interfere with the release of acetylcholine from cholinergic nerve endings but prevent acetylcholine and similar agents from acting on the receptor sites of effector cells. Both excitatory and inhibitory cholinergic responses are antagonized, but in some areas responses to exogenous acetylcholine are blocked more readily than are those to parasympathetic nerve stimulation. The classical muscarinic blocking agents are alkaloids obtained from a variety of plants including *Atropa belladonna*, *Datura stramonium*, *Hyoscyamus niger*, *Scopolia carniolica*, *Mandragora officinalis*, *Duboisia myoporoides*, etc., which belong to the order Solanaceae (potato family). (See 2,3,5.) These alkaloids are esters of tropic acid and a complex organic base. In addition to their ability to block muscarinic responses, they have important actions on the central nervous system. As a rule, the natural alkaloids and their synthetic substitutes have qualitatively similar pharmacological properties, but the ratio between the several actions may vary considerably. The central nervous system effects of some compounds are so prominent that their muscarinic blocking activity is considered of minor importance (p. 16).

## SOLANACEOUS ALKALOIDS AND DERIVATIVES

The most important solanaceous alkaloid is **atropine**, U.S.P. XIV (67) (Vol. 1, p. 479), the tropic acid ester of tropine. It is a racemic mixture of *hyoscyamine* (levo-



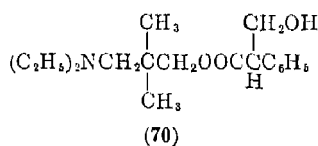
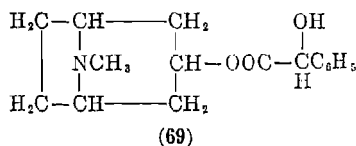
rotatory) and its dextro isomer, which is less active. Esters of the base tropine are called *tropeines*, while esters of the analogous base scopine are called *scopines*. **Scopolamine**, U.S.P. XIV, (hyoscyne, 68) is the levorotatory tropic acid ester of scopine;



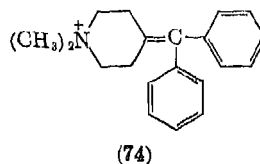
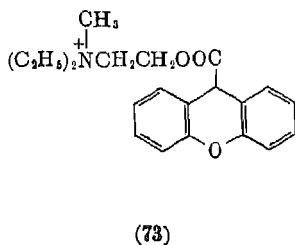
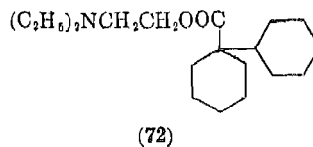
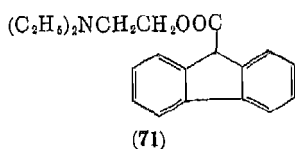
*atropine* is the racemic mixture analogous to atropine. In the presence of alkali, hyoscyamine and scopolamine are readily converted to the stable racemic forms. The muscarinic blocking activity of scopolamine is similar to that of atropine, but its effects on the central nervous system are more prominent. Quaternary derivatives of these substances, such as **atropine methyl nitrate** (Eumydrine), or **scopolamine methyl bromide** (Pamine), usually possess greater muscarinic blocking potency than the parent alkaloid when injected. However, they penetrate various membranes, such as the cornea, less readily, and their central nervous system actions are much less prominent because they pass the blood-brain barrier poorly. See also *Antispasmodics*.

#### SYNTHETIC MUSCARINIC BLOCKING AGENTS

Hundreds of synthetic compounds have been studied as possible substitutes for the solanaceous alkaloids. (See 2,17,22,51.) Only a few will be mentioned here. Many of these agents have a direct musculotropic relaxant action as well as a muscarinic blocking action. They thus combine some of the pharmacological actions of atropine with those characteristic of the smooth muscle relaxant papaverine (see Vol. 1, p. 491; Vol. 2, p. 106; Vol. 3, p. 223). The most useful synthetic agents in this category are esters. Esters of tropine with organic acids other than tropic acid, such as **homatropine**, U.S.P. XIV (tropine ester of mandelic acid, 69), and **homatropine methyl bromide**, U.S.P. XIV, N.N.R. (tropine methobromide ester of mandelic acid, Novatrine), have pharmacological properties similar to those of atropine. Aminoalkyl



esters of tropic acid such as **amprotropine** (tropic acid ester of 3-diethylamino-2,2-dimethyl-1-propanol, Syntropan, 70) have less muscarinic blocking activity and more musculotropic activity than the solanaceous alkaloids do. The same is true of most aminoalkyl esters of other aryl aliphatic acids such as **adiphenene** (2-diethylaminoethyl diphenylacetate, Trasentin),  $(\text{C}_2\text{H}_5)_2\text{NCH}_2\text{CH}_2\text{OOCCH}(\text{C}_6\text{H}_5)_2$ , although **oxyphenonium** ( $\alpha$ -phenyl- $\alpha$ -cyclohexylglycolic acid ester of methyldiethyl(2-hydroxyethyl)ammonium, Antrenyl),  $(\text{C}_2\text{H}_5)_2\text{N}^+(\text{CH}_3)\text{CH}_2\text{CH}_2\text{OOCCH}(\text{C}_6\text{H}_5)(\text{C}_6\text{H}_{11})\text{OH}$ , has a preponderance of muscarinic blocking activity. Several aminoalkyl esters of alicyclic carboxylic acids also have useful direct antispasmodic properties. These include **pavatrine** (2-diethylaminoethyl 9-fluorencarboxylate, 71) and **dicyclomine** (2-diethylaminoethyl 1-cyclohexylcyclohexanecarboxylate, Bentyl, 72). The quaternary carboxylic acid derivatives **methantheline**, N.N.R. (2-diethylaminoethyl 9-xanthene-



carboxylate methobromide, Bantline, **73**), and **promethantheline** (2-diisopropylaminoethyl 9-xanthencarboxylate methobromide, Probanthine) act predominantly as muscarinic blocking agents rather than direct smooth muscle relaxants. They also possess ganglionic blocking activity. Their pharmacological properties are similar to those of the quaternary atropine derivatives, but the latter are considerably more potent. Another synthetic antispasmodic with pharmacological properties similar to those of methantheline is **diphenmethanil** (*N,N*-dimethyl-4-piperidylidenediphenylmethane methosulfate, Prantal, **74**). See also *Antispasmodics*.

#### USES OF MUSCARINIC BLOCKING AGENTS

Muscarinic blocking agents are widely used as antispasmodics and as inhibitors of gastric secretion in the treatment of peptic ulcer, and as antispasmodics in the treatment of many conditions involving pain arising from the gastrointestinal tract, uterus, etc. The effectiveness of this form of therapy is severely limited by the fact that many features of these conditions are not amenable to anticholinergic therapy; for example, the gastrointestinal tract is capable of maintaining activity even after the administration of very large doses of muscarinic blocking agents, the pain in dysmenorrhea is probably not due to cholinergically induced contraction of the uterus, etc. In addition, troublesome side effects limit the dose employed to that which can produce only minimal inhibition of gastric secretion and minimal relaxation of the involved organs. All the natural and synthetic muscarinic blocking agents have a similar pattern of activity on various organs. Salivary secretion is most sensitive to blockade, and inhibition of ocular accommodation also occurs commonly with doses lower than those necessary to produce much relaxation of visceral organs. Minor differences in selectivity, which have been exploited in advertising claims, are probably not of great clinical importance.

Atropine or scopolamine is used routinely to decrease respiratory tract secretions prior to the administration of a general anesthetic. They are almost ideal for this purpose, and they also tend to antagonize the respiratory depression due to concomitantly administered narcotics. Scopolamine is sometimes employed during labor to promote amnesia. The central nervous system effects of several of the muscarinic blocking agents are also exploited in the treatment of Parkinsonism (p. 16). The solanaceous alkaloids and a few of the synthetic blocking agents, such as homatropine, are applied locally to the eye to produce mydriasis and cycloplegia during ophthalmic procedures.

### Ganglionic Blocking Agents

Cholinergic stimulants possessing nicotinic properties are usually equally effective on skeletal muscle and on autonomic ganglia (p. 27). However, most blocking agents are effective at only one of these loci. Curare alkaloids (p. 39) block autonomic ganglia in doses only moderately higher than those effective at the skeletal neuromuscular junction and nicotine is effective at both loci, but most autonomic ganglionic blocking agents have little or no effect on skeletal muscle responses. Nicotine was the first ganglionic blocking agent to be studied. It stimulates at low and blocks at high concentrations. The nicotine blockade is at first due to depolarization of the ganglion cells, but it later takes on the characteristics of a competitive action (p. 38). Most other ganglionic blocking agents inhibit without prior stimulation, and the blockade appears to be due entirely to competition with acetylcholine.

All the currently available ganglionic blocking agents inhibit transmission through both sympathetic and parasympathetic ganglia. The adrenal medulla is embryologically and pharmacologically comparable to autonomic ganglia, and the release of sympathomimetic amines from this organ is blocked in the same manner as ganglionic transmission, although higher doses of blocking agents may be required. The ganglionic blocking agents also inhibit axon reflexes and carotid chemoreceptor discharge, although the structures involved are anatomically dissimilar. Minor differences in effectiveness on various ganglia have been reported for several agents. However, no selectivity of practical importance has yet been demonstrated. The problem of selectivity is continuing to receive attention, as it would be most desirable to have available agents which could selectively block the sympathetic or parasympathetic system, or even more limited areas within these two major divisions. The limited selectivity of ganglionic blocking agents already reported and other known differences in the physiological and pharmacological characteristics of different ganglia suggest that it may be possible to develop suitably selective agents.

The response of an intact animal or man to ganglionic blockade is dependent upon the level of autonomic activity at the time of administration; for example, if the heart rate is slow and under vagal control it will increase following blockade, if it is fast and under sympathetic control it will decrease. Dilatation of peripheral vessels and relaxation of the gastrointestinal musculature are consistent responses to ganglionic blockade, as these structures are almost always predominantly controlled by the sympathetic and parasympathetic nervous systems respectively.

### TETRAETHYLAMMONIUM

The ability of the tetraethylammonium ion to block ganglionic transmission has been known for many years, but only recently has it been studied intensively (6,21). Blockade is due to competition with acetylcholine and is not preceded by stimulation. With minor exceptions, which are difficult to interpret, all autonomic pathways are blocked. However, relatively large doses of tetraethylammonium are required to produce complete blockade, and the maximum doses employed in man (500 mg. intravenously) appear to produce only about 50% blockade of most ganglia. Tetraethylammonium occupies a special position among the large number of onium compounds which have been studied pharmacologically (46). Compounds with 3 or more methyl groups exhibit both muscarinic and nicotinic stimulant properties (p. 28) and, in common with compounds containing larger substituents, block neuromuscular trans-

mission when administered in large doses. Tetraethylammonium possesses some neuromuscular blocking activity, but this is much less than that of most other onium compounds. In animals under artificial respiration, it has been found that several times the usual lethal dose of tetraethylammonium is required to produce skeletal muscle relaxation. Other actions of tetraethylammonium include respiratory depression with large doses, stimulation of peripheral nerve, and a poorly understood effect leading to the relief of several types of pain. (See 59.) See also *Quaternary ammonium compounds*.

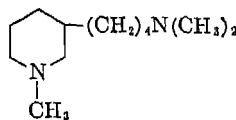
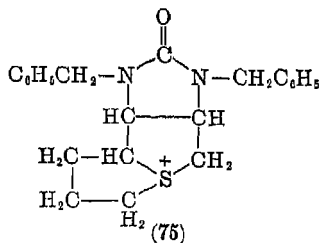
#### BISAMMONIUM COMPOUNDS

The best-known members of this group are **bis(trimethylammonium) compounds** in which the quaternary nitrogens are separated by a polymethylene chain of varying length. Ganglionic blocking activity appears in the trimethylene compound, is maximal in the penta- and hexamethylene compounds, and is largely replaced by a skeletal neuromuscular blocking action in the decamethylene compound (p. 40). However, the distance between the cationic charges is not decisive for ganglionic blocking activity, as maximal potency has been found at the 4- and 10-carbon chain lengths in series possessing other *N*-substituents (25,88). Blocking activity is not materially altered by interposing a nitrogen in the hydrocarbon chain as in **Pendiomide** ([[(methylimino)diethylene]bis[ethyldimethylammonium]],  $(\text{CH}_3)_2\text{N}^+(\text{C}_2\text{H}_5)(\text{CH}_2\text{CH}_2\text{N}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{N}^+(\text{C}_2\text{H}_5)(\text{CH}_3)_2$ .

**Hexamethonium**, N.N.R. (hexamethylenebis(trimethylammonium)),  $(\text{CH}_3)_3\text{N}^+-(\text{CH}_2)_6-\text{N}^+(\text{CH}_3)_3$ , has a ganglionic blocking action 10 to 20 times as potent as that of tetraethylammonium and a considerably longer duration of action. It is a highly specific agent and has few pharmacological actions other than ganglionic blockade. Although minor differences in the sensitivity of various ganglia to hexamethonium have been reported, both sympathetic and parasympathetic ganglia are effectively blocked. Tolerated doses of hexamethonium can produce essentially complete blockade of autonomic ganglia in man. (See 65.)

#### MISCELLANEOUS GANGLIONIC BLOCKING AGENTS

A few **thiophanium derivatives** including **Arfonad** (*l*-3,4(1',3'-dibenzyl-2'-oxoimidazolido)-1,2-trimethylenethiophanium, Ro 2-2222 or Nu 2222, 75) are effective, short-acting ganglionic blocking agents (69). However, they also appear to produce



direct peripheral vasodilatation and to cause the release of histamine and perhaps heparin. Several series of **tertiary amines** have recently been synthesized and studied for blocking activity in the hope that they might be more readily absorbed after oral administration than the quaternary agents are. Compounds such as **1-methyl-3-( $\omega$ -dimethylaminobutyl)piperidine** (W.R.L. 51-143, 76) and ***N,N*-bis(2-diethylamino-**

**ethyl)-N'-diethylamino-1,3-propanediamine** (Su-2347),  $(\text{C}_2\text{H}_5)_2\text{NCH}_2\text{CH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{N}(\text{C}_2\text{H}_5)_2)_2$ , appear to be effective ganglionic blocking agents and to be more readily absorbed than the quaternaries. However, the details of their pharmacology have not yet been elucidated. Many other highly diverse compounds have been shown to exert ganglionic blocking activity. These include procaine, quinidine, meperidine, methadone, atropine, sparteine, piperidine derivatives, sympathomimetic amines, and general anesthetics. However, these agents are not specific in their action, and inhibition of ganglionic transmission occurs only with doses which produce many other pharmacological effects.

#### USES OF GANGLIONIC BLOCKING AGENTS

The ganglionic blocking agents, particularly hexamethonium, have received extensive trial in the treatment of hypertension (45). They appear to be of definite value in severe cases, but the results of prolonged treatment in milder cases are often disappointing. Tolerance to the hypotensive action, probably an indication of the development of compensatory mechanisms, occurs rapidly in many cases, and unpleasant side effects are common. Hexamethonium produces a marked increase in blood flow in the extremities but has received only limited trial in the treatment of peripheral vascular disease. The ganglionic blocking agents are also employed to reduce the blood pressure during certain types of surgery. Blockade of parasympathetic ganglia has been utilized in the treatment of peptic ulcer; both gastric secretion and motility are reduced. Agents such as hexamethonium must be considered excellent pharmacological agents from the standpoint of specificity and effectiveness. However, the fact that both sympathetic and parasympathetic ganglia are blocked, while therapeutic problems almost invariably involve only one system, reduces their value in clinical medicine and increases the incidence of clinically important "side effects." (See 59,65.)

#### Skeletal Neuromuscular Blocking Agents

Neuromuscular blocking agents usually produce skeletal muscle paralysis by affecting the motor endplate, a specialized area at the junction of the nerve and muscle fiber which is very sensitive to acetylcholine. Under normal circumstances acetylcholine released upon stimulation of a somatic motor nerve depolarizes the endplate and thus initiates a wave of depolarization which spreads over the membrane of the muscle cell and elicits a contraction. The acetylcholine is rapidly hydrolyzed, and the endplate and muscle fiber repolarize prior to a subsequent response. After extensive inactivation of the true cholinesterase in the region of the motor endplate, sufficient acetylcholine may accumulate to produce persistent depolarization and hence skeletal muscle paralysis.

Two classes of neuromuscular blocking agents are of importance: (a) drugs such as tubocurarine (77) which stabilize the endplate and appear to compete with acetylcholine, and (b) drugs such as decamethonium which depolarize the endplate in a manner similar to excess acetylcholine (64). Under certain circumstances interconversion of these types may occur; that is, the blockade may at first present the characteristics of depolarization blockade, and later those of competitive blockade. However, the distinction between the two types of neuromuscular blocking agents is very important. Actions of competitive blocking agents are antagonized by cholinesterase inhibitors,

whereas those of depolarizing agents may be potentiated. The two types also exhibit mutual antagonism. Important differences between these two types of blocking agents are listed in Table VII. Skeletal muscles differ in their sensitivity to paralysis; for example, the soleus, a slowly responding, "red" muscle, is blocked more readily

TABLE VII. Factors Altering Competitive and Depolarizing Skeletal Neuromuscular Blockade.

Agent or procedure	Type of blockade	
	Competitive	Depolarizing
Anodal current	Potentiated	Antagonized
Cathodal current	Antagonized	Potentiated
Previous tetanization	Antagonized	Little effect or potentiated
Anticholinesterases		
Acetylcholine		
Potassium	Antagonized	Little effect
Ether	Potentiated	Antagonized
Tubocurarine	Potentiated	Antagonized
Decamethonium	Antagonized	Potentiated

by the competitive blocking agent tubocurarine than is the tibialis, a more rapidly reacting "white" muscle, whereas the order of sensitivity is reversed with the depolarizing agent decamethonium. Marked species differences in sensitivity are also known; man and the cat are less sensitive than rodents to tubocurarine, but more sensitive to decamethonium. Both types of agents are relatively specific in producing neuromuscular blockade. Some, particularly among the competitive agents, may produce ganglionic blockade, but only in doses greater than those required for neuromuscular blockade. The relative specificity of these substances for the skeletal muscle endplate is evidenced by the fact that many of them can be administered in several times the paralyzing dose without causing death if adequate respiratory exchange is maintained.

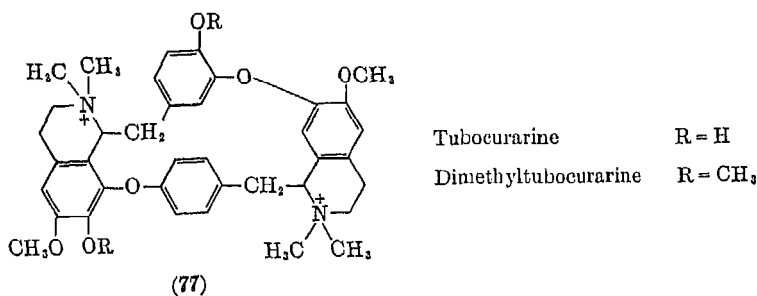
Several features of the structure-activity relation of the neuromuscular blocking agents are known (26). A cationic charge appears to be important for activity. Many tertiary alkaloids which act primarily on the central nervous system attain curare-like activity when quaternized (20). Similarly many onium salts produce neuromuscular blockade (46); tetraethyl derivatives have the least neuromuscular blocking activity, while compounds with 3 or 4 methyl substituents are the most active. With the exception of  $\beta$ -erythroidine (12) and nicotine, which produces neuromuscular blockade as one of its many diverse pharmacological effects, most neuromuscular blocking agents contain at least one quaternary nitrogen. This grouping is so characteristic of agents with neuromuscular blocking activity that one can predict that most compounds containing a quaternary nitrogen will produce a blockade if administered in sufficiently high doses. Choline itself has weak blocking activity in addition to its cholinergic stimulant properties, and simple alkyl ethers of choline exhibit predominantly blocking activity. Ethers of thiocholine and aryl ethers of choline are potent skeletal neuromuscular blocking agents.

The relation of structure to neuromuscular blocking activity in many series of bis-(quaternary) nitrogen compounds supports the view that the distance between the cationic charges is important in determining activity (8,13,50). It has long been suspected that the optimum distance between quaternary nitrogens is about 14-15 Å.,

as in tubocurarine. Compounds containing 2 trimethylammonium groups separated by a polymethylene bridge are the simplest compounds to show this relation (13,65). Maximal neuromuscular blocking activity occurs as expected with decamethonium (decamethylenebis(trimethylammonium)), whereas maximal ganglionic blocking activity occurs with pentamethonium (pentamethylenebis(trimethylammonium)) and hexamethonium (hexamethylenebis(trimethylammonium)). Further support for the importance of a distance of 14–15 Å. between the nitrogens is obtained from studies on a series of bis(dialkylaminoalkylamino)-*p*-benzoquinones (24). However, there are many potent neuromuscular blocking agents (including the toxiferine alkaloids, the most potent agents known) that contain only one quaternary nitrogen. Likewise, it is difficult to explain why many agents such as decamethonium, which have the same distance between quaternary nitrogens as tubocurarine does, produce a depolarization blockade, whereas tubocurarine produces a competitive blockade.

#### COMPETITIVE BLOCKING AGENTS

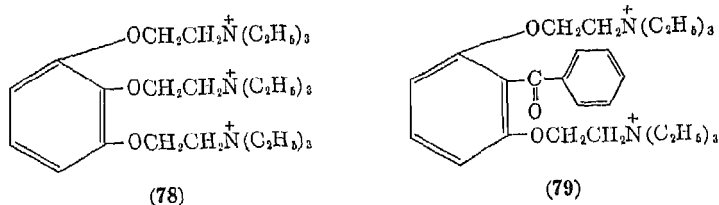
The classical example of a skeletal neuromuscular blocking agent of the competitive type is the phenolic bis(benzylisoquinolinium) alkaloid **tubocurarine**, U.S.P. XIV, N.N.R. (*d*-tubocurarine, **77**), which is obtained from the South American plant *Chondodendron tomentosum* (58) (see *Alkaloids*, Vol. 1, p. 490; *Anesthetics*, Vol. 1, p. 912; *Antispasmodics*, Vol. 2, p. 107; *Quaternary ammonium compounds*, Vol. 11, p. 386). It acts on the endplate to prevent depolarization by acetylcholine. Methylation of the free phenolic hydroxyl groups of tubocurarine as in **dimethyltubocurarine**, N.N.R. (dimethyl ether of *d*-tubocurarine, Metubine, **77**), increases curariform activity, but ethylation or butylation produces less active or inactive compounds.



The **calabash curare** alkaloids, obtained primarily from *Strychnos toxifera*, include some of the most potent curariform agents known. Nearly 20 alkaloids have been isolated from this material, the most active of which is *C*-**toxiferine-I**. Its structure has not yet been elucidated, but it appears probable that a  $\beta$ - or  $\gamma$ -carboline (pyridindole) structure containing one secondary and one quaternary nitrogen is common to this and other calabash curare alkaloids (75).

The erythrina alkaloids also possess curariform properties. In contrast to most neuromuscular blocking agents, these alkaloids, of which  $\beta$ -**erythroidine** is the most readily obtained, are tertiary amines.  $\beta$ -Erythroidine (**12**) contains a tertiary nitrogen atom common to two rings, two olefinic double bonds, a lactone, and a methoxyl group.  $\beta$ -Erythroidine has central nervous system depressant activity in addition to its curariform properties. Conversion to **apo- $\beta$ -erythroidine** (**13**) eliminates curariform activity but greatly enhances interneuron depressant activity.

A synthetic agent which produces a competitive type of neuromuscular blockade is the pyrogallol ether derivative **gallamine** (1,2,3-tris(2-diethylaminoethoxy)benzene tris(ethiodide), Flaxedil, **78**). It is much less potent than tubocurarine and, in contrast to tubocurarine, has little effect on autonomic ganglia. Among neuromuscular



blocking agents, gallamine is unique in that it contains three quaternary nitrogens attached indirectly to the same ring. However, only two of these are important for blocking activity, since a related compound, **2,6-bis(2-diethylaminoethoxy)benzophenone bis(ethiodide)** (**79**) is more potent than gallamine (**66**). Apparently, an uncharged moiety such as the benzoyl group in the benzophenone derivative may help to maintain the cationic charges at an optimum distance.

#### DEPOLARIZING BLOCKING AGENTS

**Decamethonium**,  $(\text{CH}_3)_3\text{N}^+-(\text{CH}_2)_{10}-\text{N}^+(\text{CH}_3)_3$ , may be considered the type compound of the depolarizing blocking agents (Table VII). These agents reproduce the effects of large amounts of acetylcholine on the motor endplate, and consequently some stimulation prior to blockade is to be expected. Indeed, in some animals, such as amphibians and birds, decamethonium produces a sustained contracture of skeletal muscle. Decamethonium has a shorter duration of action than tubocurarine and is excreted unchanged by the kidneys. (See 65.)

Another depolarizing blocking agent of importance is **succinylcholine** ("diacetylcholine," Anectine)  $(\text{CH}_3)_3\text{N}^+\text{CH}_2\text{CH}_2\text{OOCCH}_2\text{CH}_2\text{COOCH}_2\text{CH}_2\text{N}^+(\text{CH}_3)_3$  (**83**). Its duration of action is brief because it is rapidly hydrolyzed to the monoester and finally to succinic acid and choline by nonspecific cholinesterases. Succinylcholine is highly specific in its action, and doses several times as large as those required to produce skeletal muscle paralysis may be administered without significant effects on other systems. See also *Quaternary ammonium compounds*.

#### USES OF SKELETAL NEUROMUSCULAR BLOCKING AGENTS

Neuromuscular blocking agents are widely employed to produce skeletal muscle relaxation, particularly as a supplement to general anesthesia. Their use allows considerably smaller, and therefore safer, amounts of the general anesthetic agents to be employed. The margin between peripheral muscular relaxation and respiratory paralysis is relatively small, and consequently the neuromuscular blocking agents should be used only when equipment for providing artificial respiration is readily available. Tubocurarine and dimethyltubocurarine are widely used in general anesthesia. Decamethonium has been used for the same purpose, but it now has been largely replaced by succinylcholine. The very short duration of action of succinylcholine allows precise control of the level of blockade and also makes it a useful agent in procedures requiring only brief periods of relaxation, for example, in setting fractures or reducing dislocations, and in reducing the danger of injury during electroconvulsive therapy.



### Reflex Agents

Nervous activity can be altered reflexly by stimulation of sensory (afferent) nerve fibers throughout the body. Increased nervous activity, both central and peripheral, is commonly observed in response to noxious stimuli; this provides the basis for the effect of inhalation of ammonia in conditions of collapse. Of particular interest are the effects of drugs on specialized afferent receptor areas in the thorax and neck. Reflexes arising in these areas may profoundly affect systemic blood pressure, heart rate, and respiration. Extensive studies are currently being undertaken in an attempt to employ drugs affecting these reflexes in therapeutics.

#### VERATRUM ALKALOIDS

Extracts of *Veratrum viride* and *V. album* as well as of several kindred plants contain a large number of related alkaloids (see Vol. 1, p. 502). The most important of these are esters which upon hydrolysis yield a basic component, or alkaline, and one or more organic acids. Various purified alkaloids, or concentrates containing a mixture of alkaloids, have been found to have a common property of inducing repetitive discharges in skeletal muscle and peripheral nerves. The various alkaloids also possess to varying degrees the ability to produce a digitalis-like effect on the heart and to inhibit the cardioaccelerator response to adrenergic stimuli. The repetitive discharge of afferent fibers from the heart and lungs, and to a lesser extent from the carotid sinus and aortic arch, produces a response characterized by a decrease in blood pressure, slowing of the heart, and depression of respiration. These effects are associated with reflex suppression of sympathetic nerve activity and augmentation of vagal (parasympathetic) activity. Nausea and vomiting are also common components of the response. It is of interest that the ratios of depressor/emetic actions of the many veratrum alkaloids which have been isolated are essentially the same. This observation and the fact that sympathetic and parasympathetic centers within the central nervous system are closely interconnected indicate that the prospect of finding a member of this group which will effectively reduce blood pressure without producing gastrointestinal side effects is remote. (See 28,53.)

#### MISCELLANEOUS REFLEX AGENTS

A variety of agents including **extract of mistletoe** (*Viscum album*), **serum**, **5-hydroxytryptamine**, certain **antihistaminics**, several **amidine derivatives**, **cinchoninic acid derivatives**, **adenosinetriphosphate**, and irritant vapors may induce all or part of the response described above for the veratrum alkaloids. In addition, hypoxia (low oxygen), **cyanide**, **acetylcholine**, **lobeline**, **nicotine**, and **potassium ion** may stimulate chemoreceptors which induce predominantly a rise in blood pressure and an increase in respiration. Responses to the many diverse agents listed must involve a variety of receptors and afferent nerve fibers, many of which probably do not serve a chemoreceptor function under physiological conditions. (See 29.)

#### USES OF REFLEX AGENTS

Crude extracts of *Veratrum* have received desultory attention in therapeutics for many years. Recently, partially purified extracts and pure alkaloids have undergone extensive trial in the treatment of essential hypertension and of the hypertension associated with toxemia of pregnancy. Single injections of these materials consistently

produce a hypotensive effect, but prolonged therapy is hampered by the narrow margin between hypotensive and emetic doses, and by the fact that tolerance to the hypotensive action develops quite rapidly, although the patient may become even more sensitive to the emetic action. (See 45.) Reflex actions of the other agents mentioned are not of clinical significance, although in the past small doses of cyanide have been used to measure circulation time, and lobeline is occasionally employed as a respiratory stimulant.

## Bibliography

### GENERAL REFERENCES

- (1) Bovet, D., and Bovet-Nitti, F., *Structure et Activité pharmacodynamique des Médicaments du Système Nerveux Végétatif*, Karger, Basel, 1948.
- (2) Burger, A., *Medicinal Chemistry*, Vol. I, Interscience, N.Y., 1951.
- (3) Goodman, L., and Gilman, A., *The Pharmacological Basis of Therapeutics*, Macmillan, N.Y., 1941.
- (4) Kuntz, A., *The Autonomic Nervous System*, 4th ed., Lea and Febiger, Philadelphia, 1953.
- (5) Sollmann, T., *A Manual of Pharmacology*, 7th ed., Saunders, Philadelphia, 1948.

### SPECIFIC REFERENCES

- (6) Acheson, G. H., and Moe, G. K., *J. Pharmacol. Exptl. Therap.*, **84**, 189 (1945).
- (7) Adriani, J., *The Chemistry of Anesthesia*, C. C Thomas, Springfield, Ill., 1946.
- (8) Aeschlinmann, J. A., ed., *Ann. N.Y. Acad. Sci.*, **54**, 297 (1951).
- (9) Ahlquist, R. P., *Am. J. Physiol.*, **153**, 586 (1948).
- (10) Ahlquist, R. P., Huggins, R. A., and Woodbury, R. A., *J. Pharmacol. Exptl. Therap.*, **89**, 271 (1947).
- (11) Alles, G. A., *Physiol. Revs.*, **14**, 276 (1934).
- (12) Barger, G., and Dale, H. H., *J. Physiol. (London)*, **41**, 19 (1910).
- (13) Barlow, R. B., and Ing, H. R., *Brit. J. Pharmacol.*, **3**, 298 (1948).
- (14) Benson, W. M., Stefko, P. L., and Randall, L. O., *J. Pharmacol. Exptl. Therap.*, **109**, 189 (1953).
- (15) Berger, F. M., *Pharmacol. Revs.*, **1**, 243 (1949).
- (16) Beyer, K. H., *Physiol. Revs.*, **26**, 169 (1946).
- (17) Blicke, F. F., *Ann. Rev. Biochem.*, **13**, 549 (1944).
- (18) Borison, H. L., and Wang, S. C., *Pharmacol. Revs.*, **5**, 193 (1953).
- (19) Brodie, B. B., Bernstein, E., and Mark, L. C., *J. Pharmacol. Exptl. Therap.*, **105**, 421 (1952).
- (20) Brown, A. C., and Fraser, T. R., *Proc. Roy. Soc. Edinburgh*, **6**, 556 (1869).
- (21) Burn, J. H., and Dale, H. H., *J. Pharmacol. Exptl. Therap.*, **6**, 417 (1915).
- (22) Burtner, R. R., "Antispasmodics. Derivatives of Carboxylic Acids," in Suter, C. M., *Medicinal Chemistry*, Vol. I, Wiley, N.Y., 1951, pp. 151-220.
- (23) Butler, T. C., *Pharmacol. Revs.*, **2**, 121 (1950).
- (24) Cavallito, C. J., Soria, A. E., and Hoppe, J. O., *J. Am. Chem. Soc.*, **72**, 2661 (1950).
- (25) Chou, T. C., and Elfo, F. J. de, *Brit. J. Pharmacol.*, **2**, 268 (1947).
- (26) Craig, L. E., *Chem. Revs.*, **42**, 285 (1948).
- (27) Dale, H. H., *J. Pharmacol. Exptl. Therap.*, **6**, 147 (1914).
- (28) Dawes, G. S., *J. Pharmacol. Exptl. Therap.*, **89**, 325 (1947).
- (29) Dawes, G. S., *Brit. Med. Bull.*, **8**, 324 (1952).
- (30) Domino, E. F., Pelikan, E. W., and Traut, E. F., *J. Am. Med. Assoc.*, **153**, 26 (1953).
- (31) Domino, E. F., Unna, K. R., and Kerwin, J., *J. Pharmacol. Exptl. Therap.*, **105**, 486 (1952).
- (32) Doshay, L. J., and Constable, K., *Neurology*, **1**, 68 (1951).
- (33) Doshay, L. J., Constable, K., and Fromer, S., *Neurology*, **2**, 233 (1952).
- (34) Eckenhooff, J. E., Hoffman, G. L., and Dripps, R. D., *Anesthesiology*, **13**, 242 (1952).
- (35) Eckenhooff, J. E., Schmidt, C. F., Dripps, R. D., and Kety, S. S., *J. Am. Med. Assoc.*, **139**, 780 (1949).
- (36) Ellis, S., Plachte, F. L., and Straus, O. H., *J. Pharmacol. Exptl. Therap.*, **79**, 295 (1943).
- (37) Euler, U. S. v., *Pharmacol. Revs.*, **3**, 247 (1951).

- (38) Funderburk, W. H., King, E. E., Domino, E. F., and Unna, K. R., *J. Pharmacol. Exptl. Therap.*, **107**, 356 (1953).
- (39) Funderburk, W. H., and Unna, K. R., *J. Pharmacol. Exptl. Therap.*, **107**, 344 (1953).
- (40) Goodman, L. S., and Nickerson, M., *Med. Clin. N. Amer.*, **34**, 379 (1950).
- (41) Gross, F., Tripod, J., and Meier, R., *Schweiz. med. Wochschr.*, **81**, 352 (1951).
- (42) Guedel, A. E., *Inhalation Anesthesia*, Macmillan, N.Y., 1937.
- (43) Harvey, S. C., Wang, C. Y., and Nickerson, M., *J. Pharmacol. Exptl. Therap.*, **104**, 363 (1952).
- (44) Hayes, D. W., Wakim, K. G., Horton, B. T., and Peters, G. A., *J. Clin. Invest.*, **28**, 615 (1949).
- (45) Hoobler, S. W., and Dontas, A. S., *Pharmacol. Revs.*, **5**, 135 (1953).
- (46) Ing, H. R., *Physiol. Revs.*, **16**, 527 (1936).
- (47) Ing, H. R., *Science*, **109**, 264 (1949).
- (48) Ing, H. R., Kordik, P., and Williams, T., *Brit. J. Pharmacol.*, **7**, 103 (1952).
- (49) Jacobsen, E., *Pharmacol. Revs.*, **4**, 107 (1952).
- (50) Kimura, K. K., Unna, K., and Pfeiffer, C. C., *J. Pharmacol. Exptl. Therap.*, **95**, 149 (1949).
- (51) Kirsner, J. B., and Palmer, W. L., *J. Am. Med. Assoc.*, **151**, 798 (1953).
- (52) Koelle, G. B., and Gilman, A., *Pharmacol. Revs.*, **1**, 166 (1949).
- (53) Kraye, O., and Acheson, G. H., *Physiol. Revs.*, **26**, 383 (1946).
- (54) Krueger, H., Eddy, N. B., and Sumwalt, M., *The Pharmacology of the Opium Alkaloids, Suppl.* **165**, Pts. I and II, *Public Health Repts. (U.S.)* (1941).
- (55) Lands, A. M., *Pharmacol. Revs.*, **1**, 279 (1949).
- (56) Loewi, O., *Harvey Lectures*, **28**, 218 (1932-33).
- (57) Magee, K. R., and DeLong, R. N., *J. Am. Med. Assoc.*, **153**, 715 (1953).
- (58) McIntyre, A. R., *Curare, Its History, Nature and Clinical Use*, Univ. of Chicago Press, 1947.
- (59) Moe, G. K., and Freyburger, W. A., *Pharmacol. Revs.*, **2**, 61 (1950).
- (60) Nickerson, M., *Pharmacol. Revs.*, **1**, 27 (1949).
- (61) Nickerson, M., and Gump, W. S., *J. Pharmacol. Exptl. Therap.*, **97**, 25 (1949).
- (62) Nickerson, M., and Nomaguchi, G. M., *J. Pharmacol. Exptl. Therap.*, **101**, 379 (1951).
- (63) Nickerson, M., and Nomaguchi, G. M., *J. Pharmacol. Exptl. Therap.*, **107**, 284 (1953).
- (64) Paton, W. D. M., *Anaesthesia*, **8**, 151 (1953).
- (65) Paton, W. D. M., and Zaimis, E. J., *Pharmacol. Revs.*, **4**, 219 (1952).
- (66) Pelikan, E. W., and Unna, K. R., *J. Pharmacol. Exptl. Therap.*, **104**, 354 (1952).
- (67) Pellmont, B., and Meier, R., *Helv. Physiol. et Pharmacol. Acta*, **5**, 178 (1947).
- (68) Pfeiffer, C. C., *Science*, **107**, 94 (1948).
- (69) Randall, L. O., Peterson, W. G., and Lehmann, G., *J. Pharmacol. Exptl. Therap.*, **97**, 48 (1949).
- (70) Randall, L. O., and Smith, T. H., *J. Pharmacol. Exptl. Therap.*, **103**, 10 (1951).
- (71) Roch-Besser, B., *Helv. Med. Acta*, **17**, Suppl. 27, 1 (1950).
- (72) Rosenblueth, A., *The Transmission of Nerve Impulses at Neuroeffector Junctions and Peripheral Synapses*, Technology Press, M.I.T., and Wiley, N.Y., 1950.
- (73) Rothlin, E., *Bull. Schweiz. Akad. med. Wiss.*, **2**, 249 (1947).
- (74) Sauvage, G. L., Berger, F. M., and Bockelheide, V., *Science*, **109**, 627 (1949).
- (75) Schmid, H., Ehnöther, A., and Karrer, P., *Helv. Chim. Acta*, **33**, 1486 (1950).
- (76) Schueler, F. W., and Keasling, H. H., *J. Pharmacol. Exptl. Therap.*, **103**, 222 (1951).
- (77) Slater, I. H., O'Leary, J. F., and Leary, D. E., *J. Pharmacol. Exptl. Therap.*, **104**, 168 (1952).
- (78) Stoll, A., and Hofmann, A., *Helv. Chim. Acta*, **26**, 1570 (1943).
- (79) Stoll, A., and Hofmann, A., *Helv. Chim. Acta*, **26**, 2070 (1943).
- (80) Swanson, E. E., and Chen, K. K., *J. Pharmacol. Exptl. Therap.*, **88**, 10 (1946).
- (81) Tainter, M. L., ed., *Ann. N.Y. Acad. Sci.*, **51**, 1 (1948).
- (82) Tatum, A. L., *Physiol. Revs.*, **19**, 472 (1939).
- (83) Thesleff, S., *Acta Physiol. Scand.*, **26**, 103 (1952).
- (84) Toman, J. E. P., and Goodman, L. S., *Physiol. Revs.*, **28**, 409 (1948).
- (85) Toman, J. E. P., and Taylor, J. D., *Epilepsia*, **1**, 31 (1952).
- (86) Von Oettingen, W. F., "The Aliphatic Alcohols: Their Toxicity and Potential Dangers in Relation to Their Chemical Constitution and Their Fate in Metabolism," *Public Health Bull. (U.S.)*, **281** (1948).
- (87) Whittaker, V. P., *Physiol. Revs.*, **31**, 312 (1951).
- (88) Wien, R., Mason, D. F. J., Edge, N. D., and Langston, G. T., *Brit. J. Pharmacol.*, **7**, 534 (1952).
- (89) Wikler, A., Fraser, H. F., and Isbell, H., *J. Pharmacol. Exptl. Therap.*, **109**, 8 (1953).

## Index to Stimulants and Depressants of the Nervous System

Acetophenetiden.....	15	Glyketal.....	11
Acetylcholine.....	28	Heroin.....	13
Adiphenene.....	33	Hexaethyl tetraphosphate.....	30
Aminopyrine.....	15	Hexamethonium.....	36
Amphetamine.....	19	Hibicon.....	16
Amprotropine.....	33	Homatropine.....	33
Antazoline.....	25	Homatropine methylbromide.....	33
Apo- $\beta$ -erythroidine.....	11, 39	( <i>m</i> -Hydroxyphenyl)trimethylammonium	
Arecoline.....	31	<i>N</i> -( <i>p</i> -chlorophenyl)- <i>N</i> -methyl-	
Arfonad.....	36	carbamate.....	30
Atrolactamide.....	16	Isomethadone.....	14
Atropine.....	32	Isopropylarterenol.....	20
Atropine methylnitrate.....	33	Meperidine.....	14
Barbiturates.....	9	Mephensin.....	10
Benzazoline.....	25	Mesantoin.....	15
Benzimidazole.....	10	Metopon.....	13
Benzpyrinium.....	30	Methacholine.....	28
Benztropine.....	17	Methadone.....	14
Bethanechol.....	29	Methanol.....	9
2,6-Bis(2-diethylaminoethoxy)benzo-		Methantheline.....	33
phenone bis(ethiodide).....	40	<i>N</i> -Methylmorphinan.....	13
Bromide salts.....	15	Milontin.....	16
Caffeine.....	5	Morphine and derivatives.....	12, 13
Caramiphen.....	17	Muscirine.....	31
Carbachol.....	28	Mysoline.....	16
Chloroform.....	8	Nalorphine.....	12
Chlorpromazine.....	17	Naphazoline.....	21, 25
Choline.....	28	Neostigmine.....	30
Cinchophen derivatives.....	15	Nikethamide.....	5
Codeine.....	13	Nitrous oxide.....	8
Cyclopentamine.....	21	Norepinephrine.....	19
Cyclopropene.....	8	Octamethylpyrophosphoramide.....	30
Cyrimine.....	17	Otrivine.....	21
Decamethonium.....	40	Oxyphenonium.....	33
Dibenzamine.....	23	Paramethadione.....	16
Dibutoline.....	28	Parathione.....	30
Dicyclomine.....	33	Pavutrine.....	33
Diethazine.....	17	Pendiomide.....	36
2,6-Dihydroxypropyltrimethylammonium,		Pentylene-tetrazol.....	4
cyclic acetal.....	29	Phenacemide.....	16
Diisopropyl fluorophosphate.....	30	Phenindamine.....	17
Dimethyltubocurarine.....	39	Phenobarbital.....	10, 15
Diphenhydramine.....	16	Phenoxybenzamine.....	23
Diphenmethanil.....	34	Phentolamine.....	25
Diphenylhydantoin.....	15	5-Phenyl-5-ethylhydantoin.....	15
Edrophonium.....	30	Physostigmine.....	29
Ephedrine.....	19	Pictotoxin.....	4
Epinephrine.....	19	Pilocarpine.....	31
Ergot alkaloids.....	24	Piperoxan.....	25
$\beta$ -Erythroidine.....	11, 39	Prenderol.....	11
Ethyl alcohol.....	8	Prisilidene.....	14
Ethyl chloride.....	7	Promethanetheline.....	34
Ethyl ether.....	8	Propionylcholine.....	28
Ethylene.....	8	Prosympul.....	26
<i>O</i> -Ethyl- $\beta$ -methylcholine.....	29	4-(2-Pyridyl)butyrophenone.....	11
Ethynorepinephrine.....	20	Racemorphan.....	14
Furtrethonium.....	31	Reserpine.....	18
Gallamine.....	40	Salicylates.....	15

Scopolamine.....	33	Theophylline.....	5
Scopolamine methylbromide.....	33	C-Toxiferine-I.....	39
Strychnine.....	5	Trihexyphenidyl.....	17
Succinylcholine.....	40	Trimethadione.....	15
Tetraethylammonium.....	35	Tuaminoheptane.....	21
Tetraethyl pyrophosphate.....	30	Tubocurarine.....	39
Tetraethylthiuram disulfide.....	8	Veratrum alkaloids.....	41
Thebaine.....	13	Vinyl ether.....	8
Theobromine.....	5		

**STODDARD SOLVENT.** See Vol. 5, p. 216; Vol. 10, p. 167.

## STOICHIOMETRY

Stoichiometry is the application of the law of conservation of matter and the chemical laws of combining weights to chemical processes. These laws may be applied to reactions carried out under controlled conditions in the laboratory and to the more complex processes usually occurring in the industrial plant. The techniques are the same in either case. However, the application of the techniques is usually considerably more complicated in industrial practice than it is in the analytical laboratory, and emphasis is therefore placed here on the stoichiometry of industrial operations. In its broadest sense, stoichiometry is a system of accounting applied to the matter and energy taking part in a process involving physical or chemical change. It is a system of calculations which permits a surprisingly large amount of information to be obtained from a seemingly small number of facts.

In processes operating continuously and in steady state, the total quantity of input items must balance the total quantity of output items. Material and energy balances may be made over the entire process or over a fractional part of the process. They may be made for the sum of all the components, for any one component, or for any element in the process. Each balance will result in one equation, and there must be as many *independent* equations as there are unknowns in the process.

**Basic Principles.** The law of conservation of matter states that matter can be neither created nor destroyed, but only altered in form. (The usual form of the law of conservation of matter must necessarily be modified slightly when dealing with radioactive phenomena, but even then the correction is usually slight.) The strength of this law stems from the fact that no exceptions to it have ever been found. It forms the basis for our entire system of quantitative analysis and is of fundamental importance in almost all industries. Though this fundamental law is concerned with units of mass, when applying it to processes involving chemical change it is frequently convenient to use the mole as the unit of quantity. The laboratory chemist uses the gram mole, that is, that weight in grams numerically equal to the molecular weight; the chemist in an industrial plant often prefers the larger unit, the pound mole, that is, that weight in pounds numerically equal to the molecular weight. Frequently one speaks of a gram mole (a pound mole) of aluminum or silicon or some other solid element, meaning of course a gram atom (or pound atom) of the element in question.

Just as basic as the law of conservation of matter is the first law of thermodynamics—the law of conservation of energy. This law states that energy can be neither created nor destroyed, but only altered in form. This law, too, is proved by the fact that no exceptions to it have ever been found. In the light of recent developments which clearly establish the relationship of matter to energy, it becomes apparent that the law

of conservation of matter is in reality only a special case of the first law of thermodynamics in its broadest sense.

Since these laws may be applied to innumerable industries, each industry giving rise to its own problems and requiring its own particular technique for solution, the principles of stoichiometry are herein developed through a series of examples.

### Material Balances

**Simple Gas Problems.** Many industrial problems depend on the gas laws for their solution. In the familiar equation of state for a perfect gas:

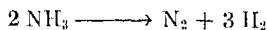
$$PV = nRT$$

where  $P$  = pressure,  $V$  = volume,  $n$  = number of moles,  $R$  = universal gas constant,  $T$  = absolute temperature, it is convenient to remember the constants involved in both c.g.s. and engineering units:

$$\begin{aligned} R &= 0.08205 \text{ (l.) (atm.)}/(^{\circ}\text{K.})(\text{gram mole}) \\ &= 1546 \text{ (cu.ft.) (atm.)}/(^{\circ}\text{R.})(\text{lb. mole}) \end{aligned}$$

The absolute temperature on the Kelvin scale,  $^{\circ}\text{K.}$ , is obtained by adding 273 to the degrees centigrade,  $t$ . The absolute temperature on the Rankine scale,  $^{\circ}\text{R.}$ , is obtained by adding 460 to the degrees Fahrenheit. One gram-mole of a perfect gas under standard conditions (1 atm. and  $0^{\circ}\text{C.}$ ) occupies 22.4 l.; the corresponding volume for 1 lb.-mole is 359 cu.ft. See also *Calculations; Gases and vapors*.

*Illustration.* When ammonia is heated to temperatures above  $900^{\circ}\text{F.}$ , it dissociates into its constituents in accordance with the equation:



The extent of the dissociation is a function of the temperature and the pressure.

A tank of liquid ammonia weighs initially 232 lb. and a pressure gage shows the contents to be at 114.1 p.s.i.a. The tank is placed in a constant temperature bath and part of the contents removed, the gas being first heated to a high temperature and then cooled. After 1,100 cu.ft. of gas (measured at  $68^{\circ}\text{F.}$  and atmospheric pressure) are withdrawn, the tank weighs 206.5 lb. Determine the per cent dissociation of the ammonia in the gas phase.

$$\text{lb.-moles NH}_3 \text{ removed from tank} = \frac{232 - 206.5}{17} = 1.5$$

If we let  $x$  = pound-moles of  $\text{NH}_3$  dissociated,  $x/2$  equals the pound-moles of  $\text{N}_2$  formed and  $3x/2$  equals the pound-moles of  $\text{H}_2$  formed. The total pound-moles present after dissociation is therefore:

$$1.5 - x + x/2 + 3x/2 = 1.5 + x$$

This gas was contained in 1,100 cu.ft. at  $68^{\circ}\text{F.}$  and 14.7 p.s.i.a. Using the pound-molar volume and correcting for temperature, we find the total number of moles to be:

$$\frac{1,100}{359} \times \frac{460 + 32}{460 + 68} = 2.86$$

from which we solve for  $x$ :

$$1.5 + x = 2.86$$

$$x = 1.36$$

$$\% \text{ dissociation} = \frac{1.36}{1.5} \times 100 = 90.7\%$$

Industrial operations in which gases are brought into contact with liquids usually involve conditions of partial saturation of the gas phase. When the gas and vapor are air and water respectively, stoichiometric problems can best be solved by using a psychrometric chart (see Vol. 1, p. 239; Vol. 5, p. 247). This chart is generally a plot of humidity, that is, amount of water vapor contained in a unit quantity of dry gas, vs. temperature for various degrees of saturation. Other properties of the wet gas which are usually superimposed on this plot are: *dewpoint temperature*, the temperature at which the gas would be saturated if cooled at constant humidity; *wet-bulb temperature*, the equilibrium temperature attained by a small amount of water brought into contact with a large amount of unsaturated air; *per cent humidity*, the percentage ratio of the weight of water carried by 1 lb. of dry air, at any temperature and pressure, to the weight of water 1 lb. of dry air could carry if saturated at that same temperature and pressure.

For systems other than air and water, psychrometric charts are not generally available. They may be constructed, however, if the volume of work can justify the time involved in their preparation.

**Solutions.** Industrial operations involving crystallization from solution give rise to problems which are amenable to graphical solution based on the solubility data or phase diagram, as demonstrated in the following example.

**Illustration.** One hundred pounds of a solution initially containing 50% naphthalene and 50% benzene are cooled to 5°C. Determine the quantity and composition of the crystals precipitated from this solution, as well as the maximum amount of naphthalene crystals which can be recovered free of benzene.

This type of problem is best solved by using the phase diagram or solubility data for the system.

Line  $AB$  (Fig. 1) represents the solubility of naphthalene, and line  $BC$  represents the solubility of benzene. Point  $B$  at 19% naphthalene is called the eutectic point and represents the particular solution with the lowest freezing point. If the initial solution represented by point 1 is cooled to 5°C. (point 2), the solid phase will contain pure naphthalene since line 1-2 crosses the naphthalene solubility curve. In other words, at about 35°C. a 50% solution of naphthalene in benzene would be saturated. Cooling below this temperature must necessarily result in precipitation of naphthalene. The quantity of crystals produced by cooling to 5°C. may be calculated by making a naphthalene balance between the crystals and mother liquor, which from the phase diagram is seen to contain 23% naphthalene.

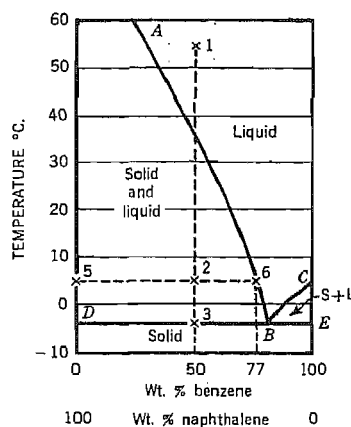


Fig. 1.

Let

$$\begin{aligned}
 x &= \text{wt. of crystals produced} \\
 x + (100 - x)0.23 &= 100(0.5) \\
 x &= \frac{100(0.5 - 0.23)}{(1 - 0.23)} \\
 x &= 35.1 \text{ lb.}
 \end{aligned}$$

It should be noted that the quantity  $(0.5 - 0.23)$  is represented on the phase diagram by the distance 2-6, whereas the quantity  $(1 - 0.23)$  is represented by the distance 5-6. Thus the same result could have been determined by taking the quotient of the appropriate line segments.

The maximum recovery of pure naphthalene from this solution is obtained when cooling is continued until the mother liquor is at the eutectic composition, point *B*. On the basis of line segments the weight of crystals at this new condition is found to be:

$$\begin{aligned}
 \text{wt.} &= 100 \left( \frac{\text{line } 3-B}{\text{line } D-B} \right) \\
 &= 100 \left( \frac{50 - 19}{100 - 19} \right) \\
 &= 38.3 \text{ lb.}
 \end{aligned}$$

This weight of pure naphthalene crystals could be recovered by cooling the solution to about  $-3.5^{\circ}\text{C}$ .

**Use of an Inert Component.** Frequently in an industrial operation, one or more materials will pass through a process unaffected by the chemical reactions taking place. One example would be the nitrogen from the air in a combustion process. The nitrogen enters the combustion zone and leaves by the stack without gain or loss, and without suffering any change. Such an inert component can be used as a key component to interrelate the inlet and exit streams. If the amount of air employed in a combustion process and the per cent of nitrogen in the flue gas are known, the total quantity of flue gas can be immediately determined.

*Illustration.* An iron ore of the following composition:  $\text{Fe}_2\text{O}_3$  76%,  $\text{SiO}_2$  14%,  $\text{MnO}$  1%,  $\text{Al}_2\text{O}_3$  9%, is smelted in a blast furnace to produce pig iron of the following analysis: Fe 94.2%, C 3.5%, Si 1.5%, Mn 0.8%. Eleven hundred pounds of coke containing 88% C and 12%  $\text{SiO}_2$  are used per ton of pig iron. Analysis of the gases shows 26% CO, 13%  $\text{CO}_2$ , and 61%  $\text{N}_2$ . It can be assumed that no iron is lost in the slag and that the slag contains 36%  $\text{CaO}$ . Determine the weight of ore and limestone (taken as pure calcium carbonate) and volume of blast air and exit gases per ton of pig iron produced.

It is apparent that the element iron can be considered a tie substance, since it exists in known percentages in both the ore and the product, pig iron, and nowhere else. It is therefore possible to determine the amount of ore required per ton of pig iron by a balance on iron:



$$\text{iron in pig} = \text{iron in ore}$$

$$(2,000)(0.942) = (\text{lb. ore})(0.76)(111.7/159.7)$$

$$\text{lb. ore} = 3,550 \text{ lb.}$$

In order to determine the amount of limestone required, it is necessary to consider the components of the slag, namely:

$$\left. \begin{array}{l} \text{MnO} \\ \text{SiO}_2 \\ \text{Al}_2\text{O}_3 \end{array} \right\} \begin{array}{l} \text{from ore} \\ \\ \end{array} \left. \begin{array}{l} \text{SiO}_2 \\ \text{CaO} \end{array} \right\} \begin{array}{l} \text{from coke} \\ \text{from flux} \end{array} \quad \begin{array}{l} \text{These components constitute 64\% of slag.} \\ \text{This component constitutes 36\% of slag.} \end{array}$$

The following individual component balances can be made:

$$\text{For MnO:} \quad \frac{3,550 \times 0.01}{70.9} - \frac{2,000 \times 0.008}{54.9} = 20.8 = 1,470$$

(moles in ore)      (moles in pig)      (moles in slag)      (lb. in slag)

$$\text{For SiO}_2: \quad \frac{3,550 \times 0.14}{50} - \frac{2,000 \times 0.015}{28} + \frac{1,100 \times 0.12}{28} = 13.56 = 675$$

(moles in ore)      (moles in pig)      (moles in coke)      (moles in slag)      (lb. in slag)

$$\text{For Al}_2\text{O}_3: \quad \frac{3,550 \times 0.04}{102} = 1.39 = 142$$

(moles in ore)      (moles in slag)      (lb. in slag)

$$\text{wt. of 64\% of the slag} = 1,470 + 675 + 142 = 2,287 \text{ lb.}$$

With CaO as the tie substance, the weight of flux, CaCO<sub>3</sub>, required per ton of pig iron is:

$$\text{lb. flux} = \frac{(2,287)(36)(56.1)}{(64)(100.1)} = 720 \text{ lb.}$$

By making a carbon balance, it is now possible to determine the volume of exit gases. Since the carbon is present in several different molecular forms, and since a gas volume is desired, it is best to make this balance on a molar basis:

$$\frac{1,100 \times 0.88}{12} + \frac{720}{100.1} = \frac{2,000 \times 0.035}{12} \text{ moles (CO and CO}_2\text{) in exit gases}$$

$$\text{moles (CO and CO}_2\text{) in exit gases} = 73.1 + 7.2 - 5.8 = 74.5$$

from which the volume of gas is found to be:

$$\text{vol.} = 359 \times 74.5 = 26,600 \text{ std. cu.ft.}$$

Obviously the nitrogen in the air and in the exit gases is an excellent tie substance for determining the volume of the air blast since:

$$\text{N}_2 \text{ in exit gases} = \text{N}_2 \text{ in air blast}$$

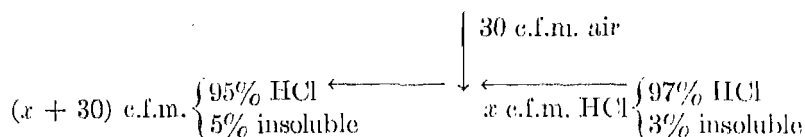
$$(26,600)(0.61) = \text{vol. of blast} (0.79)$$

$$\text{vol. of blast} = 20,500 \text{ std. cu.ft.}$$

**Dilution Metering.** Dilution metering is a relatively simple application of stoichiometry to the problem of measuring the flow of fluids. The technique is based on the addition of a foreign substance which is soluble in the fluid and is susceptible to easy quantitative measurement when so mixed. The foreign substance is added to the flowing fluid at a constant, accurately measured rate, and its concentration in the fluid is determined both upstream and downstream from the point of addition; from the concentration the rate of flow of the fluid can be readily calculated.

*Illustration.* A vacuum line carrying hydrogen chloride gas is found to contain 3% by volume of gases insoluble in water. After passing a metering section where 30 c.f.m. of air is introduced into the line, the hydrogen chloride gas is found to contain 5% by volume of water-insoluble gases. What is the rate of flow of hydrogen chloride?

At the point of addition of the diluent, the flow conditions are:



A material balance on insolubles gives:

$$0.03x + 30 = 0.05(x + 30)$$

$$x = \frac{30(1 - 0.05)}{(0.05 - 0.03)} = 30 \frac{(0.95)}{(0.02)} = 1,425 \text{ c.f.m.}$$

If care is taken to insure thorough mixing before the downstream analysis station is reached, very accurate results can be obtained. The same accuracy can be achieved, and it is sometimes more convenient to introduce a measured quantity of heat into a flowing stream. In place of chemical analysis, one merely measures the temperature both upstream and downstream from the point of addition. If the duct is well insulated between the two temperature stations, and the total temperature rise is small (so as not to alter the velocity head of the flowing fluid), a heat balance will give the desired flow rate as follows:

$$W(H_2 - H_1) = Q$$

For liquids and for perfect gases this becomes:

$$W(\text{lb. moles/sec.}) = \frac{Q \text{ (B.t.u./sec.)}}{C_p(t_2 - t_1)}$$

**Recycle Operations.** It is often useful to recycle part of a process stream from the exit end of a piece of equipment back to the inlet end. In drying certain solids, for example, the drying rate is carefully controlled by controlling the humidity of the air circulated through the drying chamber. One method of controlling this humidity is to recycle a portion of the exit wet air which, when blended with the incoming dry air, results in an air stream with the desired humidity. Another example occurs in air conditioning in the wintertime. The outside air must be both heated and humidified to bring it to the proper conditions for maximum comfort. By recycling a portion of the inside air to the fresh air inlet duct, a considerable amount of heat energy can be saved. A typical example based on a drying operation is given below.

*Illustration.* In order to insure a slow rate of drying and thereby prevent checking of the dried product, an inlet relative humidity of 70% at 75°F. is specified. The air leaving the dryer has a relative humidity of 95%. If the outside air has a dewpoint of 40°F., what fraction of the air passing through the dryer must be mixed with the outside air to provide the desired moisture content in the air fed to the dryer?

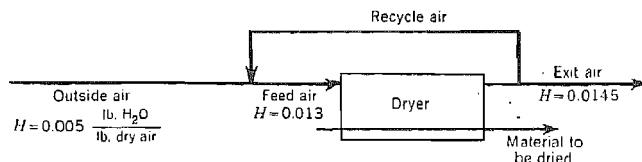
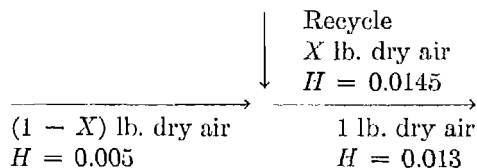


Fig. 2.

A diagram of the process flow is shown in Fig. 2. The indicated humidities are read from a psychrometric chart. In the usual case, problems involving recycle or bypass streams can be solved by making a material balance around the point where the recycle stream joins the main stream:



A material balance on water gives:

$$0.005(1 - X) + 0.0145X = 0.013$$

$$X = (0.013 - 0.005)/(0.0145 - 0.005) = 0.842$$

Thus 84.2% of the air passing through the dryer is recycled and reused.

**Countercurrent Processing.** Many extraction or washing operations are carried out stepwise with countercurrent flow of the wash liquors and the material being washed. The countercurrent nature of these operations makes it possible to wash with a minimum amount of solvent and obtain comparatively concentrated solutions as the final extract liquors.

Calculations on countercurrent washing operations usually reduce to straight material balances when three assumptions are made. These assumptions are: (1) sufficient time has been allowed in each mixer-settler unit for equilibrium to be achieved; (2) the wash liquid has been completely and uniformly mixed with the solution adhering to the surface of the solid; and (3) the solid exerts no selective adsorbing action on the solute but is completely inert.

For problems which reduce to straight material balances, it is usually sufficient to establish a number of independent equations equal to the number of unknowns of composition and mass. It is important to be certain that each of the equations established is truly independent. Any material balance equation which can be derived from other material balance equations already written cannot be regarded as an additional independent equation. The use of equations that are not truly independent generally results in proving such things as that zero equals zero. Where more independent equations can be written than are required, it becomes a matter of judgment which equa-

46097

tions should be used. In such cases the selection of the balances for calculating the unknowns should be based on those quantities which are known most precisely and will therefore introduce the minimum error. In addition, choosing the appropriate equations may result in considerable simplification of the problem. An example follows.

*Illustration.* Ten tons per hour of dry seashore sand containing 1% sodium chloride by weight are to be washed by 10 t.p.h. of salt-free water running counter-currently to the sand through two classifiers in series. Assuming perfect mixing of the sand and wash water in each classifier and assuming that the sand is discharged from each classifier containing 50% liquid (on dry basis), determine the salt content of the sand if it is dried after leaving the second classifier.

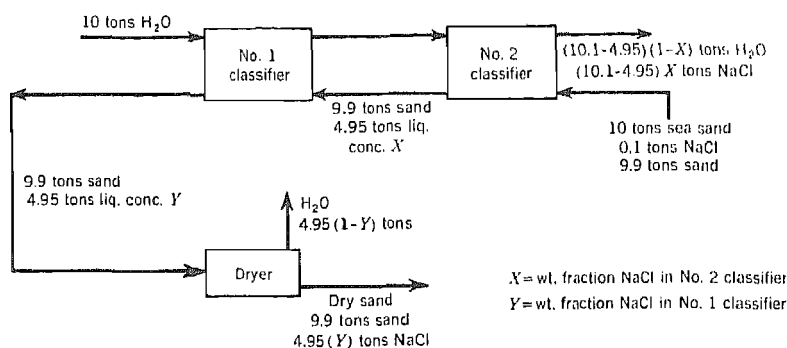


Fig. 3.

Figure 3 (basis, 1 hr.) indicates the flow streams for the washing operation employing two classifiers. The problem involves the determination of the salt concentration in the solution carried from the No. 1 classifier by the sand. This is best accomplished by making an overall salt balance as well as a salt balance on the No. 2 classifier.

Overall salt balance:

$$0.1 = 4.95Y + (10.1 - 4.95)X$$

Salt balance on No. 2 classifier:

$$0.1 + 10Y = (10.1 - 4.95)X + 4.95X$$

These equations can be simplified to:

$$0.1 = 4.95Y + 5.15X$$

$$0.1 = -10Y + 10.1X$$

which can be solved simultaneously to give  $Y = 0.00488$ , from which the hourly salt loss is found to be  $4.95Y = (4.95)(0.00488) = 0.0242$  ton, and the salt content of the dried sand is  $0.0242/9.9 = 0.24\%$  (dry basis).

**Countercurrent Process with Recycle.** Industrial operations are seldom simple idealized operations of the type shown here as examples. However, even the most complex processes can usually be shown to be combinations of simple operations. In the following example, the idea of recycle is combined with the principle of countercurrent contacting in a washing operation.

*Illustration.* One hundred thousand pounds of cotton waste containing 0.4 lb. of oil per lb. of dry waste are to be extracted per day in a two-cell continuous counter-current system. Fifty thousand gallons of oil-free gasoline, sp.gr. = 0.72 (that is, 300,000 lb.), are sent to the system per day. The waste leaving each cell contains 1.0 lb. of solution per pound of dry waste. The waste leaving the last unit is centrifuged down to 0.20 lb. of solution per pound of dry waste and the solution sent to the overflow from the last cell. How many pounds of oil are recovered per day?

Let

$x$  = lb. oil/lb. soln. in cell 1

$y$  = lb. oil/lb. soln. in cell 2

(See Fig. 4.)

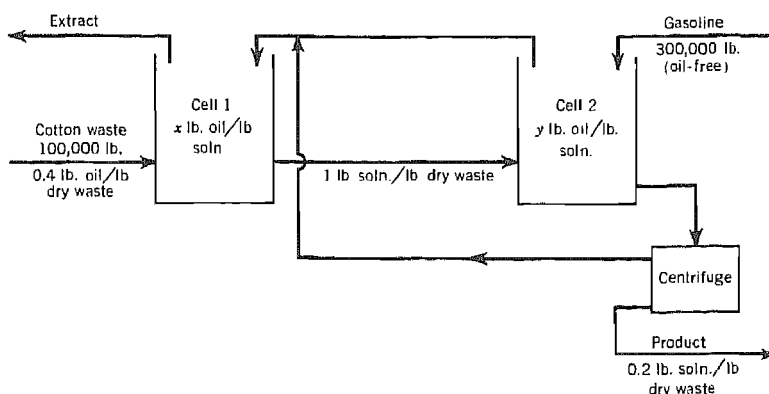


Fig. 4.

Feed contains  $100,000(0.4)/(1.4) = 28,600$  lb. oil (since 0.4/1.4 is the fraction of oil in the untreated waste).

$$100,000 - 28,600 = 71,400 \text{ lb. dry waste}$$

An overall oil balance gives:

$$28,600 = 71,400 (0.2)(y) + (300,000 + 28,600 - 71,400 \times 0.2) (x)$$

$$28,600 = 314,320x + 14,280y \quad (1)$$

An oil balance in cell 2 gives:

$$\text{oil in waste from cell 1} = \text{oil in waste from cell 2} + \text{oil in overflow}$$

$$71,400x = 71,400y + 300,000y$$

$$y = 71,400x/37,400 \quad (2)$$

Substituting equation 1 in equation 2 and solving for  $x$ :

$$28,600 = 314,320x + 14,280(71,400/37,400)x$$

$$x = 0.0905$$

Weight of oil recovered per day is  $314,320(0.0905) = 28,400$  lb.

### Energy Balance

The material balance, although of tremendous importance, is still only one part of most problems. The other part is concerned with the energy which is absorbed or liberated in every chemical reaction. The quantity of energy may be large, as in combustion reactions, or small, as in most organic syntheses. This energy usually manifests itself as heat which must be supplied to or withdrawn from the system. This gives rise to the heat balance, that is, a balance of all the heat quantities entering, leaving, generated in, or stored in a given chemical process.

There is considerable advantage in completing the material balance before attempting the heat balance. The material balance is usually simpler to complete and is more readily checked for correctness. Then, with the material balance completed, the only additional work involved in the heat balance is the evaluation of the enthalpies of each and every item appearing in the material balance.

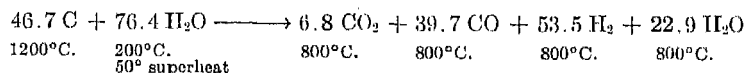
The heat of reaction is the difference between the enthalpies of the products and reactants of a chemical reaction. This heat of reaction is dependent on the chemical nature of each reacting material and also on their physical states. The standard heat of reaction is defined as the change in enthalpy of a system resulting from the reaction under 1 atm. pressure, starting and ending with all materials in their standard states of aggregation at 18°C.

Special cases of the heat of reaction are heat of formation, heat of combustion, and heat of dilution. The first represents the enthalpy change when a compound is formed from its elements. The next represents the enthalpy change when the compound is burned in air, the combustion products being cooled to 18°C. The third represents the heat effect accompanying the solution of 1 mole of solute in a specified number of moles of solvent (integral heat of solution) or the heat effect accompanying the solution of a unit mass of solute in a solution, of specified concentration, so large in amount as to result in no appreciable change of composition (differential heat of solution). Tabled values of these standard heats of formation, combustion, or solution may be found in most handbooks. See also *Thermochemistry*; *Thermodynamics*.

Two basic laws greatly simplify problems involving the use of heats of reaction. The law of Lavoisier and Laplace teaches that as much energy is required to decompose a compound into its elements as was required to form the compound from its elements. In other words, changing the direction of a chemical reaction requires that the sign be changed on the heat of reaction. The law of Hess states that the net heat change in a chemical process is the same whether the reaction takes place in one or several steps.

*Illustration.* Steam at 200°C., 50° superheat, is blown through a bed of coke weighing 6,000 lb. and initially at 1200°C. The gases leave at an average temperature of 800°C. with the following composition by volume on a dry basis: H<sub>2</sub> 53.5%, CO 39.7%, CO<sub>2</sub> 6.8%. Of the steam introduced, 30% passes through undecomposed. If the reaction must stop when the bed has cooled to 900°C., what fraction of the bed will have been consumed and what volume of water gas will have been produced? (Specific heat of coke = 0.35 B.t.u./(lb.)(°F.).) Basis, 100 lb.-moles of dry water gas.

The equation representing the chemical reaction is:



It is necessary to evaluate the enthalpy of each compound relative to a common datum. The elements in their standard states of aggregation at 18°C. being chosen as the datum, the enthalpy per mole is given by:

$$H = \Delta H_f + \sum \lambda + Cp(t - 18)$$

where  $\Delta H_f$  = heat of formation from the elements;  $Cp$  = heat capacity per mole;  $t$  = temperature of compound;  $\sum \lambda$  = sum of latent heat of phase changes occurring between 18°C. and  $t^\circ C$ .

For coke (Note.  $\beta$ -Graphite is usually taken as the standard state of aggregation for carbon. Thus coke has, strictly speaking, a heat of formation relative to  $\beta$ -graphite.):

$$H = 2,600 \times 1.8 + 0.35 \times 12 \left( \frac{1,800 - 18}{1.8} \right) = +8,850 \text{ B.t.u./lb.-mole}$$

For water (as reactant):

$$H = -68,320 \times 1.8 + 1,435 \times 1.8 + 8.13 \left( \frac{200 - 18}{1.8} \right) = -119,580 \text{ B.t.u./lb.-mole}$$

For carbon dioxide:

$$H = -94,030 \times 1.8 + 11.57 \left( \frac{800 - 18}{1.8} \right) = -163,970 \text{ B.t.u./lb.-mole}$$

For carbon monoxide:

$$H = -26,620 \times 1.8 + 7.44 \left( \frac{800 - 18}{1.8} \right) = -44,760 \text{ B.t.u./lb.-mole}$$

For hydrogen:

$$H = 7.07 \left( \frac{800 - 18}{1.8} \right) = 3,080 \text{ B.t.u./lb.-mole}$$

For water (as product):

$$H = -68,320 \times 1.8 + 1,435 \times 1.8 + 8.91 \left( \frac{800 - 18}{1.8} \right) = -121,620 \text{ B.t.u./lb.-mole}$$

The heat effect accompanying any reaction is equal to the sum of the enthalpies of all the products minus the sum of the enthalpies of all the reactants. Therefore, for the reaction written above, the heat effect is

$$\begin{aligned} \Delta H_R &= \sum H_P - \sum H_R \\ &= 6.8(-163,970) + 39.7(-44,760) + 53.5(3,080) + 22.9(-121,620) \\ &\qquad\qquad\qquad 46.7(8,850) - 76.4(-119,580) \\ &= +3,213,000 \end{aligned}$$

The positive sign indicates that heat is absorbed in this reaction. This heat must be supplied by the unreacted coke, which cools from 1200°C. to its final temperature, 900°C.

Let  $X$  = lb. coke reacted. Then by heat balance:

$$\frac{X}{(12)(46.7)} \times 3,213,000 = (6,000 - X)(0.41) \left( \frac{1,200 - 900}{1.8} \right)$$

$$X = 71 \text{ lb. coke}$$

$$(X/6,000) \times 100 = 1.185\% \text{ of original bed reacted}$$

From the original equation it is apparent that 46.7 moles of carbon produced 122.9 moles of water gas. The volume of water gas produced when 71 lb. of coke are consumed is therefore:

$$V = 122.9 \times 359 \times 71 / (12 \times 46.7) = 5,600 \text{ cu.ft. at S.T.P.}$$

or

$$V = 5,600 \times (460 + 800) / 492 = 14,350 \text{ cu.ft. at exit of coke bed}$$

### Bibliography

- (1) Hougen, O. A., and Watson, K. M., *Chemical Process Principles*, Vol. I, Wiley, N.Y., 1943.
- (2) Lewis, W. K., and Radasch, A. H., *Industrial Stoichiometry*, McGraw-Hill, N.Y., 1926.

R. F. BENENATI

**STOMACH PREPARATIONS.** See *Antianemia preparations*.

**STONEWARE, CHEMICAL.** See *Ceramics (chemical ware)*, Vol. 3, p. 575.

**STORAGE BATTERIES.** See *Batteries, electric; Cells, electric*.

**STORAX.** See *Resins, natural*, Vol. 11, p. 686.

**STOUT.** See *Beer and brewing*, Vol. 2, p. 384.

**STREPTIDINE**,  $C_6H_{18}N_6O_4$ ; **STREPTOBIOSAMINE**,  $C_{13}H_{23}NO_9$ . See *Streptomyces antibiotics (streptomycin)*.

**STREPTIN; STREPTOCIN.** See *Streptomyces antibiotics (survey)*.

**STREPTOLIN.** See *Antibiotics*, Vol. 2, p. 18; *Streptomyces antibiotics (survey)*.



## STREPTOMYCES ANTIBIOTICS

Survey.....	p. 57	Erythromycin.....	p. 94
Streptomycin.....	66	Carbomycin.....	103
Chloramphenicol.....	81	Viomycin.....	108
Neomycin.....	90		

See also *Antibiotics*; *Tetracyclines*.

## SURVEY

Among the various groups of microorganisms (*q.v.*) producing antibiotics (chemical substances which in dilute solutions have the capacity to inhibit the growth of and even to destroy other microorganisms), members of the genus *Streptomyces* occupy a unique place. Next to penicillin (*q.v.*), a product of a group of true molds, the most important antibiotics in chemotherapy discovered since 1940 are produced by species of *Streptomyces*. In this respect, this genus occupies a special position among the **actinomycetes**, since, although species of other genera in this group (notably *Nocardia*) also produce a number of antibiotics, none of these has so far found any practical application. The actinomycetes as a whole belong to the higher, or filamentous, bacteria, rather than to the true molds, but they are frequently and less precisely spoken of as "mold-like bacteria" (5,7).

The ability of an organism to produce one or more antibiotics is a strain rather than a species characteristic. Certain strains of a given organism may produce a particular antibiotic and others may not; some strains may produce one antibiotic, and other strains of the same organism are able to produce another antibiotic; for example, some strains of *Streptomyces griseus* form streptomycin; others give rise to grisein, streptocin, or candicidin; and still others are unable to form any antibiotic. The same culture may produce more than one antibiotic. The same strain of *Streptomyces fradiae*, for example, produces an antibacterial agent, neomycin, and an antifungal agent, fradidin. The same antibiotic may be produced by the same organism or by different strains in more than one form: thus streptomycin and mannosidostreptomycin are both produced by *S. griseus*.

More than 100 chemical substances or preparations that possess antibiotic properties have been isolated since 1939 from cultures of actinomycetes, mostly from species of *Streptomyces* (1,17). Most of these substances have been found in the culture broth, and a few in the mycelium of the organisms. They vary greatly in their physical and chemical properties, antimicrobial spectra, toxicity to animals, and chemotherapeutic potentialities. Some of these antibiotics are characterized by very wide spectra, being active against both bacteria and fungi, or against Gram-positive, Gram-negative, and acid-fast bacteria, or against bacteria and larger viruses; others have narrower spectra, being active only against certain Gram-positive bacteria, or against yeast-like fungi; still others have very narrow spectra, and are active only or largely against certain limited groups of organisms, such as mycobacteria or certain viruses. Antibiotics vary not only qualitatively, or in the nature of the organisms that are sensitive to them, but also quantitatively, or in the concentrations of each required to affect different organisms (2,3,4,6,8,12).

Of the antibiotics produced by actinomycetes, about 10 have already found application in the treatment of human and animal infectious diseases. These include streptomycin, U.S.P. XIV, N.N.R., and its derivative dihydrostreptomycin, N.N.R..

chlortetracycline (Aureomycin), N.N.R., chloramphenicol (Chloromycetin), U.S.P. XIV, N.N.R., oxytetracycline (Terramycin), N.N.R., tetracycline (Achromycin, Tetramycin), neomycin (Mycifradin), N.N.R., erythromycin (Ilotycin, Erythrocin), N.N.R., carbomycin (Magnamycin), N.N.R., and viomycin (Viocin, Vinaetin). These antibiotics are used in the treatment of a great variety of infections, caused largely by Gram-positive and Gram-negative bacteria, mycobacteria, rickettsiae, some of the larger viruses, and certain protozoa. Some antibiotics, such as streptomycin and cycloheximide (acetidione), have also found application in the treatment of plant diseases. Cycloheximide is also used in the diagnostic laboratory.

The isolation of these antibiotics has been a result of extensive screening programs carried out in numerous university and industrial laboratories throughout the world, mostly, however, in the United States (9). Large numbers of cultures of actinomycetes were isolated from soils, composts, river bottoms, peat materials, and other natural substrates. They were tested systematically against different bacteria, fungi, and other microorganisms, various media and different conditions of culture being used. Although these screening programs antedated 1939, no true antibiotic was isolated before that date; enzyme-like preparations, designated "actinomycetes lysozyme" and "actinomycetin," were obtained, but their chemotherapeutic potentialities were not recognized.

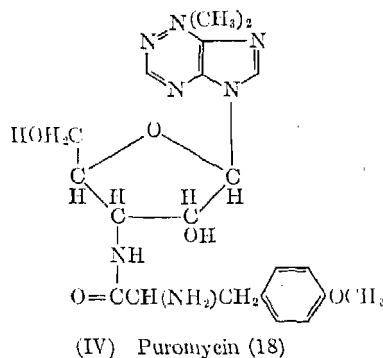
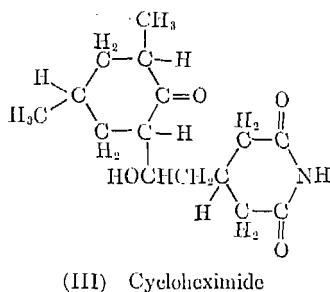
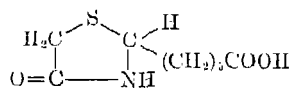
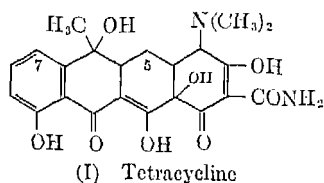
The first true antibiotic from an actinomycete, *actinomycin*, was isolated from a culture of an actinomycete in 1940 by Waksman and Woodruff (14,15). The first antibiotic that possessed chemotherapeutic possibilities was isolated by the same workers (16) two years later, and was called *streptothricin*. This antibiotic possessed remarkable physical, chemical, and biological properties, such as solubility in water, basic nature, stability to heat, limited toxicity, and definite activity against Gram-positive and Gram-negative bacteria. However, streptothricin proved too toxic to be used widely but it did point to the possibility of obtaining from actinomycetes other antibiotics with similar properties but less toxicity to animals. A year later, in 1943, streptomycin was isolated, the first actinomycete antibiotic to find extensive practical application as a chemotherapeutic agent (10,11). See also *Antibiotics*, Vol. 2, pp. 17-19.

Since then, hundreds of thousands of cultures have been tested for their ability to produce antibiotics. In view of the fact that 10-60% of all freshly isolated cultures are able to inhibit the growth of bacteria, fungi, and other microorganisms, the possibility of finding promising substances is very great. Unfortunately, the usefulness of these substances as chemotherapeutic agents is controlled by their toxicity to animals and their particular antimicrobial spectra. To become a useful agent, a new substance must be less toxic than others already known or be effective against organisms resistant to other antibiotics already in use.

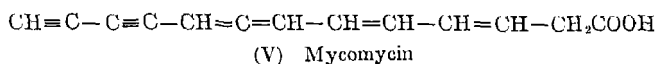
### Classification

The *Streptomyces* antibiotics represent a large variety of chemical compounds. Formulas (I-IV) show all the completely known structures of *Streptomyces* antibiotics (1) except for streptomycin and related antibiotics (see p. 66) and chloramphenicol (see p. 81); oxytetracycline is 5-hydroxytetracycline and chlortetracycline is 7-chlortetracycline (C.A. numbering, Formula I). These compounds differ greatly in their physical properties, including solubility in water and in organic solvents; sta-

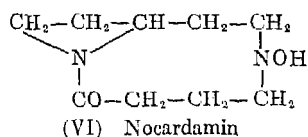
bility; their chemical properties, notably composition, reactivity, and stability; their antimicrobial activities, both *in vivo* and *in vitro*; and their toxicity to animals. The



formulas for mycomycin (V) and nocardamin (VI) are also included, although these compounds are produced not by a *Streptomyces*, but by species of *Nocardia* (there is some question with regard to mycomycin, however). Various difficulties are involved



in the classification of these antibiotics, especially since many of the substances have not been crystallized and some have not even been sufficiently described.



The logical basis for a broad classification of antibiotics is their antimicrobial spectra, or ranges of activity against different organisms. The following is a summary of a system of classification of *Streptomyces* antibiotics (including mycomycin), in which several broad groups are recognized. There is, of course, considerable overlapping among these groups, and often a particular substance may be placed with as much justification in one group as in another. There are also a number of antibiotic preparations obtained from species of *Streptomyces* and other actinomycetes that do not fit readily into any of these groups, but may be closely related to one or more of them (17). Thus *thioaurin* is active against both Gram-negative and Gram-positive bacteria, and *actithiazic acid* and *nocardamin* are active only against mycobacteria (Gram-positive, acid-fast).

Certain species or strains of *Streptomyces* are also able to produce substances that

are active against neoplasms (tumors), but these are still insufficiently evaluated. It is not even known whether they are to be considered true antibiotics.

#### SUBSTANCES ACTIVE PRIMARILY AGAINST GRAM-POSITIVE BACTERIA

**The actinomycin group** comprises substances that are soluble in organic solvents and to only a limited extent in water. They are active largely against Gram-positive bacteria and to a much lesser extent against Gram-negative bacteria and fungi. Many of them are pigmented, ranging from red and orange to yellow. Most of them are highly toxic to animals. Here belong not only the actinomycins but also the *xanthomycins*, *resistomycin*, *rhodocidin*, and a number of other preparations.

**The acid-base indicator group** members change their color depending on the reaction of the substrate. Many of them are quinones or anthocyanins. Here belong the *rhodomycins*, *rhodomycetin*, *actinorhodin*, *litmocidin*, and *coelicolorin*.

**The viomycin group** antibiotics are basic polypeptides which contain guanidine or creatinine or both. They include the *vinactins* and viomycin, which are active mainly against mycobacteria.

**The erythromycin-carbomycin group** members are active largely against Gram-positive bacteria, rickettsiae, larger viruses, and certain Gram-negative bacteria, such as members of the genus *Haemophilus*. They have no activity against fungi and the smaller viruses. They are basic compounds of limited toxicity. They include erythromycin, carbomycin, and *leucomycin*.

#### SUBSTANCES ACTIVE AGAINST GRAM-POSITIVE AND GRAM-NEGATIVE BACTERIA

**The streptothricin group** members are active not only against bacteria, but also slightly against fungi. They are nonpigmented, basic substances, readily soluble in water and insoluble in most organic solvents, and they contain amino acids. They possess a certain delayed toxicity to animals. This group includes the streptothricins, the *streptolins*, *streptin*, *actinorubin*, *pleocidin*, and others.

**The streptomycin group** members are active against a large number of bacteria and actinomycetes, but not against fungi and viruses. They are nonpigmented, basic substances, soluble in water and insoluble in most organic solvents. They give maltol or isomaltol on alkaline hydrolysis (see p. 69) and are inactivated by cysteine. They are not readily absorbed from the digestive system and possess only limited toxicity to animals. Here belong streptomycin and related compounds *mannosidostreptomycin* and *hydroxystreptomycin*. The chemically reduced form of streptomycin, *dihydrostreptomycin*, is not inactivated by cysteine and has not been found, as yet, as a natural product. *Dextromycin* appears to be a closely related compound.

**The neomycin group** is active against Gram-positive and Gram-negative bacteria, but not against fungi or viruses. Members of this group are nonpigmented, basic substances, soluble in water, and insoluble in organic solvents. They are not readily absorbed from the digestive system and have a toxic auditory effect when given parenterally, but are relatively nontoxic when given orally or used topically. They can be differentiated chemically from the previous two groups in that their molecules do not include amino acids as do those of the streptothricin group, and they are not inactivated by cysteine as the streptomycin group is; and biologically by their antimicrobial spectra, especially by the use of resistant bacterial strains. Here belong the neomycins, *catenulin*, and *flavomycin*.

**The chloramphenicol-tetracycline group** members are active against Gram-

positive and Gram-negative bacteria, rickettsiae, and larger viruses, but not against fungi and smaller viruses. They are relatively nontoxic and can be readily absorbed from the digestive system. They are neutral or amphoteric, soluble in organic solvents and, to a more limited extent, in water. They include chloramphenicol, chlortetracycline, oxytetracycline, tetracycline, and flaveolin. See also *Tetracyclines*.

#### SUBSTANCES ACTIVE PRIMARILY AGAINST FUNGI

The group active against both bacteria and fungi contains a variety of different substances. The most important of these are *thiolutin*, *mycomycin*, *musarin*, and *helixin*.

The group not active against bacteria has as its best-known members *nystatin*, *fungicidin*, *rimocidin*, *ascosin*, *candicidin*, *fradycin*, *antimycin A*, and *cycloheximide*.

#### SUBSTANCES ACTIVE AGAINST VIRUSES AND PHAGES

These substances are not active against bacteria or fungi. They appear to be highly selective in their action. Little is known concerning their nature, mode of action, and utilization. They include *ehrliehin*, *abikoviromycin* and *phagolessin*.

Some antibiotics, like *netropsin*, appear to be active against certain viruses, such as vaccinia virus.

#### SUBSTANCES ACTIVE MAINLY AGAINST PROTOZOA

These substances are active selectively against various pathogenic protozoa, such as trichomonads, trypanosomes, and amebas. Some are also active against certain bacteria, notably cocci and other Gram-positive bacteria, or against yeasts. They include *anisomycin*, *trichomycin*, and *streptocin*. Other compounds having marked antifungal or antibacterial activity also have antiprotozoal activity, such as thiolutin, chlortetracycline, and oxytetracycline. Two substances, *puromycin* and *borellidin*, show a marked activity against Trepanemataceae.

### Preparation

The various steps leading to the isolation and characterization of an antibiotic are outlined in Figure 1. It is absolutely necessary that media and equipment be kept free from contaminating organisms at all times. See "Heat sterilization" under *Sterilization*.

The screening methods used by various laboratories in the search for new antibiotics are variations of the following basic method. Soil samples are plated out on a nutrient medium which is solidified by the addition of agar and which is more or less selective for actinomycetes. One such medium is the egg albumin agar:

Glucose.....	10	g.
K <sub>2</sub> HPO <sub>4</sub> .....	0.5	g.
MgSO <sub>4</sub> ·7H <sub>2</sub> O.....	0.2	g.
Fe <sub>2</sub> (SO <sub>4</sub> ) <sub>3</sub> ·9H <sub>2</sub> O.....	1.0	mg.
Egg albumin.....	0.15	g.
Agar.....	15.0	g.
Distilled water.....	1	liter
pH.....	7.2	

(The egg albumin is dissolved in a minimum amount of 0.1 N NaOH.)

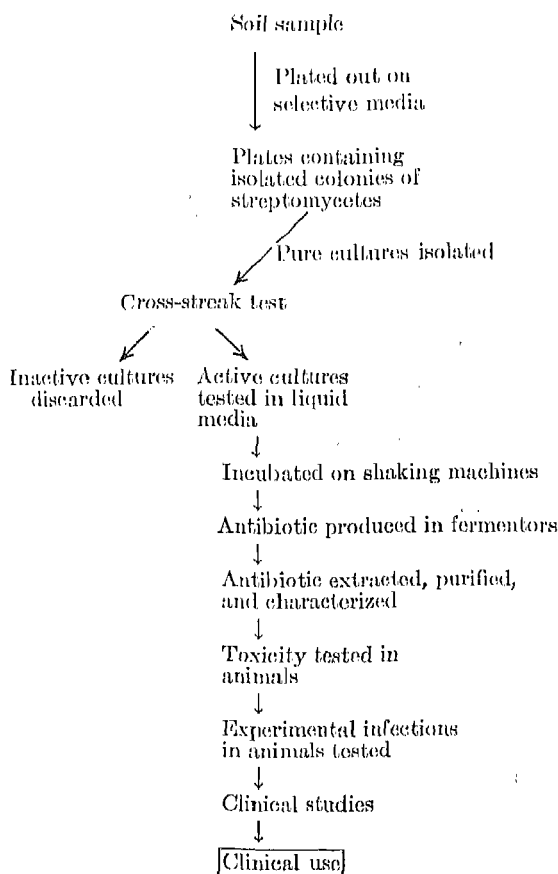


Fig. 1. Isolation and characterization of a *Streptomyces* antibiotic.

From the plates of such selective media, pure cultures of streptomycetes can be isolated and kept on slants of various media. One of the best all-around media for the cultivation of these organisms is the yeast-extract glucose agar:

Yeast extract.....	10 g.
Glucose.....	10 g.
Agar.....	15 g.
Tap water.....	1 liter
pH.....	6.5-7.5

The isolated cultures are tested for their antibiotic activity by the *cross-streak test*: The *Streptomyces* is first streaked on a solid nutrient medium and incubated until good growth is obtained (3-5 days at 28°C.). The test organisms for which antibiotics are sought are now cross-streaked perpendicularly to the streptomycete growth. After a suitable period of incubation, designed to permit the growth of the test organisms, the production of an antibiotic is indicated by a sterile zone around the growth of the *Streptomyces*. The cultures showing antibiotic activity against test organisms can now be selected for further studies. Once the test organisms that the antibiotic is effective against are known, valuable leads to the possible identity of the antibiotic produced can be obtained by cross-streaking the culture against varieties of these test organisms that have acquired resistance to known antibiotics.

Next, the antibiotic observed on the agar plates has to be produced in liquid media. The first step in production consists in obtaining active broths (also called "beers" in the industry) in small flasks of nutrient solutions incubated on shaking machines. (The shaking machines are designed to increase the aeration of the liquid cultures. Two types of shaking machines are on the market, the rotary type and the reciprocal type. The results obtained on rotary shakers are usually easier to duplicate than those obtained on reciprocal shakers.) The next step consists in producing the antibiotic in fermentors in large enough quantity for clinical work.

There is no universal medium on which all antibiotics can be produced. For every antibiotic, optimum physical conditions, such as aeration, agitation, pH of the medium, and temperature of incubation, must be determined. The streptomycetes, in order to produce any antibiotic, have to be supplied with suitable sources of carbon and nitrogen. Certain trace elements such as zinc, iron, manganese, or magnesium must be present, and, depending on the organisms and the antibiotic, some special nutrients, such as vitamins or special precursors, may have to be supplied (7). So far, the selection of complex organic or synthetic media suitable for the production of an antibiotic has been an empirical process consisting in trying a variety of nutrients. Such trials can, of course, utilize experience gained in developing media for the known antibiotics.

The following are examples of media used for the production of some of the *Streptomyces* antibiotics:

(1) *Corn steep liquor medium for actithiazic acid:*

Corn steep liquor.....	10	g.
Peptone.....	5	g.
Glucose (Cereulose).....	10	g.
CaCO <sub>3</sub> .....	1	g.
Tap water.....	1	liter
pH.....	7.0	

(2) *Soybean meal medium for oxytetracycline:*

Soybean meal.....	3%
Corn starch.....	0.5%
Casein hydrolyzate (N-Z-Amine B).....	0.1%
Sodium nitrate.....	0.3%
Calcium carbonate in tap water.....	0.5%
pH.....	7.0

(3) *Medium for thioaurin:*

(NH <sub>4</sub> ) <sub>2</sub> HPO <sub>4</sub> .....	0.4%
NaCl.....	0.5%
K <sub>2</sub> HPO <sub>4</sub> .....	0.2%
MgSO <sub>4</sub> ·7H <sub>2</sub> O.....	0.1%
FeSO <sub>4</sub> ·7H <sub>2</sub> O.....	0.002%
ZnSO <sub>4</sub> ·7H <sub>2</sub> O.....	0.001%
MnCl <sub>2</sub> .....	0.0002%
Glucose.....	1.0%
Yeast extract.....	0.1%
In distilled water.	

(4) *Asparagine medium for candididin:*

Asparagine.....	1.0%
Glucose.....	1.0%
Sodium lactate.....	0.5%
K <sub>2</sub> HPO <sub>4</sub> .....	0.05%
MgSO <sub>4</sub> ·7H <sub>2</sub> O.....	0.02%
Fe <sub>2</sub> (SO <sub>4</sub> ) <sub>3</sub> ·9H <sub>2</sub> O.....	0.001%
ZnSO <sub>4</sub> ·7H <sub>2</sub> O.....	0.001%
In distilled water, pH 7.3	

## EXTRACTION AND PURIFICATION

Since the various antibiotics are very different chemically, extraction methods differ from group to group. Before extraction is attempted, consideration should be given to the stability of the antibiotic, which can be roughly determined by "streak-dilution assays" (13) of active broth aliquots subjected for various lengths of time to various temperatures under various pH conditions. When stability is determined, a method of extraction can be devised which will not unduly destroy the antibiotic substance.

Antibiotics can be extracted and purified by two different types of methods: (1) utilization of their solubility properties, including solvent extraction and precipitation as salts or derivatives, and (2) adsorption and elution from various materials.

**Solvent Extraction.** Examples in which solubility properties are used are:

*Thioaurin Extraction.* The filtered broth is extracted with ethyl acetate and this extract is concentrated *in vacuo*. The tarry aqueous residue is dissolved in carbon tetrachloride and the solution is extracted with water. The active substance is back-extracted with ethyl acetate. After concentration *in vacuo*, cooling causes crystallization. Recrystallization is possible from acetone.

*Actinomycin Extraction.* The broth is extracted with ether and the extract is concentrated *in vacuo*. Crystallization of actinomycin occurs when acetone is added to the ether concentrate.

**Adsorption and Elution.** Other antibiotics such as streptothricin can be successfully extracted and purified by using only adsorption procedures.

The ion-exchange resins are useful tools for the extraction and purification of many antibiotics, such as neomycin (see p. 90).

*Streptothricin Extraction.* After adsorption at pH 8.0 on charcoal, streptothricin can be eluted with a mixture of 49.2% water, 50% methanol, and 0.80% formic acid. The eluate is concentrated *in vacuo*, and crude streptothricin is precipitated by the addition of acetone. The crude material can be purified by repeated chromatography over charcoal using methanol to load the column and to elute it.

## CHARACTERIZATION

The characterization of an antibiotic involves the determination of all its properties, physical, chemical, and biological.

**Physical and Chemical Properties.** The physical and chemical properties which have to be studied in order to characterize an antibiotic include its solubility in various solvents, its stability at various temperatures under various pH conditions, its inactivation by various substances, and its various chemical reactions. Certain antibiotics such as fradecin, rimocidin, nystatin, and candididin have characteristic absorption spectra in ultraviolet light. Others such as streptomycin are optically active.



Two very useful tools which are used extensively to characterize antibiotics are paper chromatography and countercurrent distribution. The latter method can also be used in the purification of antibiotics.

The ultimate aim of the chemical study of an antibiotic is the elucidation of its structure and, if possible, its synthesis. Of the actinomycetes antibiotics that have found practical application, chloramphenicol is the only one produced by synthesis on a commercial scale.

**Microbiological Properties.** Antibiotics can be tested in solutions at any stage in production either by dilution methods or by diffusion methods (see Vol. 2, pp. 8-9).

The range of microbiological activity or the antimicrobial spectrum of an antibiotic can be determined *in vitro* for the bacteria, mycobacteria, fungi, and those protozoa which can be grown in bacteria-free cultures by *dilution methods*. The streak-dilution assay (13) in a solid medium has been used successfully in the development of many antibiotics.

*Diffusion assays* such as the cup diffusion and paper disk methods should be used only when the characteristics of the studied antibiotics are well known. Certain antibiotics, such as candidin, do not diffuse readily in agar and, although they are very active by dilution methods, exhibit very little activity if tested by many of the diffusion methods.

The activity of antibiotics against rickettsiae, viruses, and many protozoa can be determined by more elaborate methods.

Most microorganisms can develop resistance to antibiotics to which they are exposed. For most antibiotics, this development of resistance is a slow, gradual process; development of resistance to streptomycin and grisein, on the other hand, can be a very rapid process.

**Pharmacological Properties.** The toxicity of an antibiotic is determined first in laboratory animals: mice, guinea pigs, and rabbits. The *acute toxicity* is the damage caused by a single dose of the antibiotic; the *chronic toxicity*, the damage caused by repeated doses over a period of time.

The *in vivo* activity of antibiotics is determined first in experimental infections of laboratory animals. If the difference between the toxic doses of an antibiotic and the therapeutic doses is large enough, the antibiotic may be tried clinically.

### Uses

At present, only a handful of *Streptomyces* antibiotics are used clinically.

The clinical role of streptomycin is well established. Streptomycin is used mainly in the treatment of infections caused by Gram-negative bacteria and in the treatment of tuberculosis. Streptomycin and dihydrostreptomycin have very similar clinical action but differ in the type of their toxic effect.

Oxytetracycline and chlortetracycline are two compounds having about the same clinical value. They can be administered orally or topically for the treatment of a variety of infections caused by Gram-positive and Gram-negative bacteria. They are also used in the treatment of amebiasis and rickettsial infections. Tetracycline is also active against these infections and is thought to have an efficacy similar to oxy- and chlortetracycline.

Chloramphenicol has about the same uses as the tetracyclines but is especially effective in the treatment of typhoid fever. It is not used in the treatment of amebiasis.

Neomycin, because of its great stability and nonirritability, is used topically in the treatment of bacterial infections of the skin. Since neomycin is not absorbed from the intestine, it is used as an intestinal disinfectant either presurgically or in the treatment of bacterial intestinal infections. The rather high toxicity of neomycin limits its systemic use to bacterial infections caused by organisms that are resistant to the less toxic chemotherapeutic agents.

Erythromycin and carbomycin are two recently developed chemotherapeutic agents. These antibiotics can be used orally in the treatment of rickettsial diseases and in the treatment of bacterial infections caused by Gram-positive bacteria.

Viomycin is an antibiotic of very limited application. It should be used only in the treatment of tuberculous cases not responding to other forms of therapy.

### Bibliography for Survey

- (1) Benedict, R. G., *Botan. Rev.*, **19**, 229 (1953).
- (2) Burkholder, P. R., *J. Bacteriol.*, **52**, 503 (1946).
- (3) Krassilnikov, N. A., and Koreniako, A. I., *Mikrobiologiya*, **8**, 673 (1939).
- (4) Kuroya, M., et al., *J. Antibiotics (Japan)*, **B2**, 37 (1949).
- (5) Lieske, R., *Morphologie und Biologie der Strahlenpilze*, G. Borntraeger, Leipzig, 1921.
- (6) Nakhimovskaya, M., *Microbiologiya*, **6**, 131 (1937).
- (7) Perlman, D., *Botan. Rev.*, **19**, 46 (1953).
- (8) Rowatt, J. W., et al., *Antibiotics and Chemotherapy*, **1**, 185 (1951).
- (9) Routien, J. B., and Finlay, A. C., *Bacteriol. Revs.*, **16**, 51 (1952).
- (10) Schatz, A., Bugie, E., and Waksman, S. A., *Proc. Soc. Exptl. Biol. Med.*, **55**, 66 (1944).
- (11) Waksman, S. A., Bugie, E., and Schatz, A., *Proc. Staff Meetings Mayo Clinic*, **19**, 537 (1944).
- (12) Waksman, S. A., Horning, E. S., Welsch, M., and Woodruff, H. B., *Soil Sci.*, **54**, 281 (1942).
- (13) Waksman, S. A., and Reilly, H. C., *Ind. Eng. Chem. (Anal. Ed.)*, **17**, 556 (1945).
- (14) Waksman, S. A., and Woodruff, H. B., *Proc. Exptl. Biol. Med.*, **45**, 609 (1940).
- (15) Waksman, S. A., and Woodruff, H. B., *J. Bacteriol.*, **42**, 231 (1941).
- (16) Waksman, S. A., and Woodruff, H. B., *Proc. Soc. Exptl. Biol., N.Y.*, **49**, 207 (1942).
- (17) Waksman, S. A., and Lechevalier, H. A., *Guide to the Actinomycetes and Their Antibiotics*, Williams and Wilkins, Baltimore, 1954.
- (18) Waller, C. W., Fryth, P. W., Hutchings, B. L., and Williams, J. H., *J. Am. Chem. Soc.*, **75**, 2025 (1953); Baker, B. R., Joseph, J. P., and Williams, J. H., *ibid.*, **76**, 2838 (1954); Baker, B. R., Schaub, R. E., Joseph, J. P., and Williams, J. H., *ibid.*, **76**, 4044 (1954).

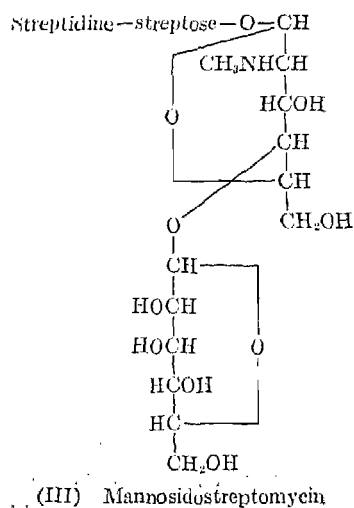
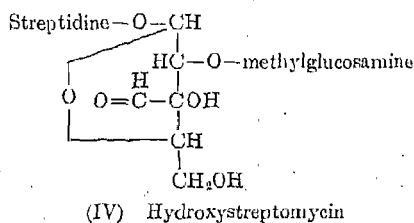
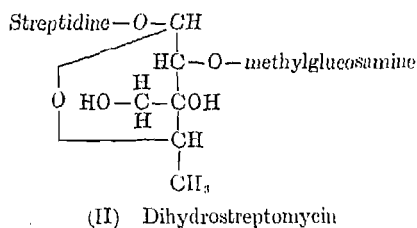
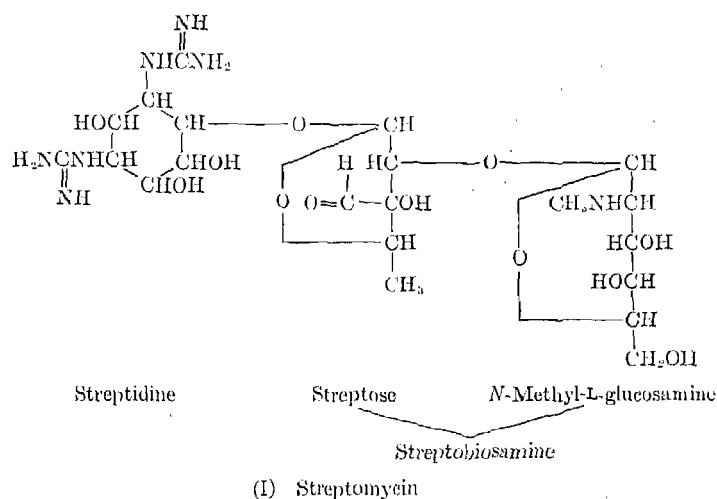
SELMAN A. WAKSMAN AND H. A. LECHEVALIER

### STREPTOMYCIN

Streptomycin (I), U.S.P. XIV, N.N.R.,  $C_{21}H_{39}N_7O_{12}$ , is an antibiotic produced by certain *Streptomyces*, mainly *S. griseus*. It is basic in nature, soluble in water, and thermostable. Streptomycin is a nonpigmented substance. It is produced commercially in the form of its inorganic salts, mainly the sulfate,  $2C_{21}H_{39}N_7O_{12} \cdot 3H_2SO_4$ , and the hydrochloride-calcium chloride double salt ("calcium chloride complex"),  $2(C_{21}H_{39}N_7O_{12} \cdot 3HCl) \cdot CaCl_2$ , as amorphous white powders. It is also produced in the reduced form, dihydrostreptomycin (II) (usually as the trihydrochloride or the sulfate), which has not yet been found as a natural product.

Streptomycin and dihydrostreptomycin are mainly active against Gram-positive, Gram-negative, and acid-fast bacteria, such as mycobacteria, and they are chiefly used in the treatment of infections caused by Gram-negative bacteria and mycobacteria. They are successful chemotherapeutic agents in the treatment of infections

of the urinary tract, tularemia, brucellosis, granuloma inguinale, plague, certain respiratory infections, and tuberculosis. They are not active against true fungi, in distinction to streptothricin, or against rickettsiae and larger viruses, as distinguished from other antibiotics such as the tetracyclines (*q.v.*). Organisms sensitive to streptomycin can become resistant to this antibiotic upon continued contact either in culture media or in the animal body.



Not only streptomycin but also certain related compounds (mannosidostreptomycin (III) and hydroxystreptomycin (IV)) are produced by various species of *Streptomyces*, most important of which is *S. griseus*. This organism is widely distributed in the soil and in other natural substrates. Not all strains of this organism are able to produce streptomycin. The streptomycin-producing capacity of an organism can be increased by strain selection and by development of suitable media.

**History.** Although streptomycin-producing cultures of *S. griseus* and of other streptomycetes have now been isolated from different natural substrates, strains

developed from the original culture isolated first in 1943 in the laboratories of the Department of Microbiology of the New Jersey Agricultural Experiment Station, Rutgers University, are largely used throughout the world for the manufacture of streptomycin.

Following the isolation of actinomycin in 1940 and of streptothricin in 1942, investigators in the Department of Microbiology of Rutgers University succeeded in obtaining from a smear of a chicken's throat and from a New Jersey soil a strain of *S. griseus* which had the capacity to produce a new antibiotic, closely related to streptothricin in its physical and general microbiological properties, but differing from it in its chemical properties, antimicrobial spectrum, and toxicity to animals. It was designated "streptomycin," after the new generic name *Streptomyces*, created a few months previously by Waksman and Henrici; its isolation was announced in January, 1944 (24). Streptomycin was purified by chromatography by Carter *et al.* (3), Kuehl *et al.* (15) and others. The formula of streptomycin was definitely established by Kuehl *et al.* in 1946 (14), and dihydrostreptomycin, the first chemical derivative made, was prepared that same year (21).

Streptomycin proved to be highly effective in the treatment of a large number of infectious diseases, including tularemia, fowl typhoid, plague, and chancreoid, brought about in experimental animals by various Gram-negative and Gram-positive bacteria. Before the end of 1944, Feldman and Hinshaw (6) had demonstrated its effectiveness in experimental tuberculosis of guinea pigs, and streptomycin was being submitted to clinical trials.

Wide-scale distribution of streptomycin began in 1946, and a program of clinical research was instituted by the concerted efforts of the United States government, the manufacturers of streptomycin, the National Research Council Committee on Chemotherapy, and civilian medical scientists. The Committee on Chemotherapy supervised and coordinated the first large-scale series of investigations on the use of streptomycin in the treatment of bacterial infections. The first thousand clinical cases were thus evaluated (11). A variety of human and animal diseases caused by various bacteria were found to respond readily to streptomycin treatment. In 1946 also, Hinshaw, Feldman, and Pfuetze (8) reported observations on the first 100 cases of tuberculosis treated with streptomycin. Further studies brought out the fact that various forms of tuberculosis respond promptly to treatment with streptomycin.

Within 4 years of the beginning of the wide-scale distribution, streptomycin production had grown into a large industry with a monthly output of more than 15,000 kg. of the pure base.

### Physical and Chemical Properties

Streptomycin, as the free base, as the hydrochloride and sulfate salts, and as the calcium chloride complex, is extremely soluble in water. The base is insoluble in organic solvents, such as ether, chloroform, and acetone. The hydrochloride is completely soluble in methanol, less soluble in ethyl alcohol and virtually insoluble in *n*-butyl alcohol, acetic acid, and pyridine. The sulfate is only slightly soluble in methanol and virtually insoluble in the other organic solvents. Streptomycin is odorless or almost so and has a slightly bitter taste. Most of the salts are hygroscopic and deliquesce on exposure to air.

Aqueous solutions of the salt are levorotary:  $[\alpha]_D^{25} -84^\circ$  ( $c = 1\%$ ) for the hydrochloride and  $[\alpha]_D^{25} -76^\circ$  ( $c = 1\%$ ) for the hydrochloride-calcium chloride double salt.

Both streptomycin and dihydrostreptomycin are extremely stable and resistant to the action of most enzymes (9,22).

The streptomycin molecule is composed of three parts; *streptidine*, *streptose*, and *N-methyl-L-glucosamine*, joined to one another by glycosidic linkages. The glycosidic linkage between the streptidine and streptose moieties of streptomycin is much weaker than that between the streptose and *N-methyl-L-glucosamine* portions. Consequently, streptomycin may be cleaved by a variety of reagents to yield streptidine plus the streptose and *N-methyl-L-glucosamine* moieties which are still joined glycosidically as a disaccharide, called *streptobiosamine* (16). See Formula I.

One of the products of alkaline hydrolysis of streptomycin is maltol (3-hydroxy-2-methyl- $\gamma$ -pyrone; 3-hydroxy-2-methyl-4*H*-pyran-4-one (C.A.)),  $\text{O.C(CH}_3\text{):C(OH).CO.CH:CH}$ , which has also been isolated from the bark of certain trees. It originates

from the streptose portion of the streptomycin molecule. This rearrangement of the streptose moiety to maltol takes place only when the aldehyde group at carbon 1 is glycosidically combined, and when the C-3 aldehyde group is free. The other products of the hydrolysis depend upon the conditions of the reaction.

Acid hydrolysis of streptomycin, on the other hand, yields furfural, which also arises from the streptose moiety. Here too the other products depend upon the conditions of the hydrolysis.

Streptomycin shows three basic groups on titration.

The property of forming a crystalline double salt with calcium chloride,  $2(\text{C}_{21}\text{H}_{39}\text{N}_7\text{O}_{12} \cdot 3\text{HCl}) \cdot \text{CaCl}_2$ , is specific for streptomycin and is not shared by the impurities likely to be present in crude concentrates.

In addition to the three basic groups, streptomycin contains a reactive carbonyl (aldehyde) group. Its presence was shown by the inactivation of the antibiotic by carbonyl group reagents, and by the preparation of streptomycin oxime and semicarbazone (2). Hydrogenation of the aldehyde group to an alcohol group gives **dihydrostreptomycin**, U.S.P. XIV, N.N.R.,  $\text{C}_{21}\text{H}_{41}\text{N}_7\text{O}_{12}$ . The reaction may be carried out in water solutions with platinum oxide or palladium black as a catalyst under hydrogen pressures below 20 p.s.i. Both the crystalline calcium chloride complex and pure streptomycin hydrochloride have been hydrogenated successfully. Since dihydrostreptomycin does not form a crystalline calcium chloride complex, the use of streptomycin - calcium chloride complex for the preparation of dihydrostreptomycin requires the removal of calcium either before or after the hydrogenation step. Dihydrostreptomycin is more stable than the streptomycin and does not respond to any of the carbonyl reactions characteristic of streptomycin. Also, unlike streptomycin, dihydrostreptomycin does not form maltol on alkali treatment. This difference can be used to measure the course of hydrogenation and the quantity of streptomycin in samples of dihydrostreptomycin.

Titus and Fried (28) subjected streptomycin concentrates to countercurrent distribution and reported evidence of the presence in the material of a substance other than streptomycin. The second substance was separated from streptomycin chromatographically and was isolated as the crystalline reineckate by Fried and Titus (7). This substance, which is somewhat less active against various bacteria than is streptomycin, was initially named "streptomycin B," but was renamed *mannosidostreptomycin* (III) as a result of more recent structural investigations. Catalytic hydrogenation of this antibiotic gave *dihydromannosidostreptomycin*.

### Preparation and Manufacture

Streptomycin is produced by growing certain streptomycin-producing strains of *S. griseus*, a sporulating actinomyceete, in suitable media. The original culture was a very poor producer in comparison with the production strains used today. These production cultures can be considered genetically as mutants derived from the Rutgers strain. The various methods used to obtain these production strains are: natural selection, selection in presence of streptomycin, ultraviolet light irradiation, and x-ray irradiation. By such methods, producing strains able to form 2000  $\gamma$ /ml. of streptomycin were obtained (4).

*S. griseus* is susceptible to actinophage attack. Actinophages are viruses that are obligatory parasites of the actinomyceete cells (33) and are closely related to bacteriophages. They destroy the *S. griseus* cells and thus prevent the formation of streptomycin. Strains of *S. griseus* resistant to actinophage attack can be selected by subjecting a population of the organism to the phage and by isolating the unlysed colonies of the actinomyceete.

Streptomycin is produced in the best yields by fermentation on submerged cultures aerated by shaking or by forcing air through, since the oxygen demand of these cultures is high. It can also be produced in stationary cultures, but the yields are low because of lack of aeration.

In stationary cultures, growth of *S. griseus* reaches a maximum in 10 days, whereas maximum growth in submerged cultures is usually attained in 3-5 days. This is followed by lysis of the mycelium. Growth of the organism is accompanied by a gradual increase in alkalinity of the culture, due to the formation of ammonia and amino nitrogen. Production and accumulation of streptomycin parallel growth of the organism, reaching a maximum when lysis just sets in; this is followed by a decrease when the rate of lysis reaches a maximum (31,34).

During the *growth phase*, the organism forms extensive mycelium, accompanied by a reduction in the soluble nitrogen, inorganic phosphate, and available carbohydrate. Some lactic acid is at first produced and then consumed; the oxygen demand is high, and little streptomycin is produced. During the second or *autolytic phase of growth*, streptomycin is produced actively, and the pH of the medium rises; the quantity of mycelium is decreased as a result of lysis. An excess of phosphorus in the medium has a depressive effect upon growth of the organism and upon streptomycin production.

Streptomycin can be produced in the laboratory both on complex organic and on synthetic media. The first complex organic medium used had the following composition: glucose, 10 grams; peptone, 5 grams; meat extract, 5 grams; NaCl, 5 grams; tap water, 1000 ml. On such a medium yields of about 100  $\gamma$ /ml. were obtained. Now many superior complex organic media have been developed (36,37,40). One such medium has the following composition: glucose, 1%; distiller's solubles, 2%; NaCl, 1%; NaNO<sub>3</sub>, 0.5%; K<sub>2</sub>HPO<sub>4</sub>, MgSO<sub>4</sub>·7H<sub>2</sub>O, FeSO<sub>4</sub>·7H<sub>2</sub>O, and CaCl<sub>2</sub>, in amounts totaling 0.3%; tap water. With it, broths containing about 250  $\gamma$ /ml. can be obtained in 3-5 days. Another medium containing soybean meal, a substance which is very effective in the production of streptomycin, has the following composition: soybean meal, 4%; glucose, 2.5%; distiller's solubles, 0.5%; NaCl, 0.25%; tap water.

The composition of a synthetic medium permitting streptomycin production, is: L-proline, 15 grams; glucose, 10 grams; NaCl, 5 grams; K<sub>2</sub>HPO<sub>4</sub>, 2 grams; MgSO<sub>4</sub>·7H<sub>2</sub>O, 1 gram; CaCl<sub>2</sub>, 0.4 gram; FeSO<sub>4</sub>·7H<sub>2</sub>O, 20 milligrams; ZnSO<sub>4</sub>·7H<sub>2</sub>O, 10 milligrams; in 1 liter of distilled water, final pH of 7.0.

In the laboratory streptomycin is produced in Erlenmeyer flasks that are aerated by shaking or in small fermentors (5–10 gal.). In industry, large fermentors with a capacity of 10,000–20,000 gal. are used.

Shaking machines may be of two different types: rotary shakers or reciprocal shakers. In both, the flasks are fixed on a board by special clamps. With the rotary shaking machine the board describes a circle in the horizontal plane so that the liquid in the flasks is swirled around and thus aerated. With the reciprocal shaking machine, the table is moved back and forth, the liquid being aerated as it crashes against the walls of the flasks every time the direction of motion is reversed.

Fermentors are closed containers which are partly filled with the nutritive medium. Agitation of the liquid mass is accomplished by stirrers and baffle plates (23). Aeration is accomplished by forcing, through the fermentation liquid, air that has been sterilized by passage through filters to remove air-borne organisms.

Several types of equipment for aeration are now commonly used. These include the open-pipe sparger, the sintered-glass aerator, and horizontal pipes containing small openings along their lengths. The air is introduced at the bottom of the fermentor and the action of the agitator effects even distribution throughout the medium.

To avoid foaming, air and agitation must be kept at a proper balance, since too much air causes excessive foaming and too little inhibits microbial growth. For control of foaming, a surface-activating substance which is nontoxic to the organism and does not interfere with recovery and purification is used; it must be sterilized before addition to the fermentor. Certain oils such as lard oil and certain silicones can be used as antifoams.

Sterility of equipment and medium is essential for satisfactory fermentation. Sterilization (*q.v.*) is accomplished by heating the medium in the fermentor to 120°C. and maintaining this temperature for one-half hour before cooling to 25°C. Continuous sterilization of medium has been successfully demonstrated and may have some economic advantage. To maintain the aseptic conditions necessary for fermentation, all equipment must be designed to avoid pockets, which may serve as breeding places for contaminating organisms. All piping and equipment must be connected to high-pressure steam lines for sterilization.

Although the actual detailed procedures for the commercial production of streptomycin are not published, the following general outline will give an idea of the manipulations involved.

The producing culture is usually kept in stock by drying spores in sterile soil. *Inoculation* is usually carried out as follows: An agar slant is inoculated with a small quantity of the stock culture and is incubated, under carefully controlled conditions, until sporulation occurs. The spores are then suspended in sterile distilled water, and the suspension is transferred to a shake flask plugged with cotton and containing about 300 ml. of nutrient solution. The flasks are placed on a shaking machine in a temperature-controlled room (25–30°C.). The laboratory culture is thus transferred through a series of increasingly larger fermentors, each vessel being so designed that it will provide the required quantity of growing organisms or inoculant for efficient utilization of the next larger fermentor. The medium at the beginning of fermentation is neutral, but the pH usually rises to 8 or even 8.5 as fermentation progresses. The temperature is kept at about 25°C. by circulating temperature-controlled water through jackets or coils built into the fermentor.

The fermentation cycle varies from one to several days depending upon the culture,

the medium, and the environmental conditions. Yields ranging from 500 to 2000  $\gamma$ /ml. are usually obtained.

Although vitamin B<sub>12</sub> (cyanocobalamine) is produced by *S. griseus* together with streptomycin, this vitamin is at present mainly produced separately from streptomycin with the use of specially selected B<sub>12</sub>-producing mutants of *S. griseus*. Different media are also used to obtain maximum yields of the vitamin. See *Vitamins*.

**Extraction and Purification.** Streptomycin does not lend itself readily to a solvent-extraction process of isolation from broth. Recovery on an adsorbent, such as charcoal or ion-exchange resins, is the basic concentration step in most practical processes. Streptomycin can, however, be extracted by use of solvent systems containing a carrier. Such a method may be briefly described as follows: The streptomycin broth is extracted at pH 6.5 with *n*-butyl alcohol containing 10% lauric acid as a carrier. The streptomycin is picked up by the solvent system, but back extraction with water at pH 2.0 again brings the streptomycin into aqueous solution. This aqueous solution is evaporated to dryness *in vacuo* at pH 5.0. The dry residue is extracted with methanol at pH 2.0. Streptomycin having a potency of 823  $\gamma$ /mg. is precipitated out of the methanol solution by the addition of acetone, with an overall yield, for the whole process, of 82% (27).

In the isolation of streptomycin by adsorption, a preliminary step is the separation of the mycelium from the broth by filtration. In large-scale operation the most successful filtration procedure consists in the use of a continuous-pressure filter. The broth is acidified with hydrochloric or sulfuric acid to pH 2-4, stirred with charcoal (Norit A, Nuchar C-190-H, or Darco G-60) and the mixture filtered. At this low pH streptomycin is not adsorbed and is stable for considerable time. After this pretreatment operation, the clarified, decolorized filtrate is neutralized to pH 7.0-7.5 and is ready for separation of the antibiotic.

Streptomycin can be adsorbed on charcoal and eluted with acidified alcohol or can be adsorbed on a cation-exchange resin such as IRC50, the elution being carried out with dilute mineral acid. The acid can be removed by anion-exchange resins such as IR4B or IRA400. If the antibiotic is left in the form of the free base, neutralization with mineral acids will yield the corresponding salt.

The potency and the quality of the crude streptomycin are related to the activity of the broth. Crude products ranging in potencies from 200 to 600  $\gamma$ /mg. with yields of 30-65%, have been reported.

Since carbon is a relatively nonspecific adsorbent, a great many other substances, some of which are toxic, are isolated along with streptomycin. This fact makes necessary further fractionation before the drug is safe for therapeutic use. Improvements in the purification steps have been developed and applied successfully to production. The commercial products available at present are virtually pure chemical compounds. Industrial isolation procedures based on absorption methods have been patented (38,39).

Chromatography (*q.v.*) has proved to be an invaluable tool in the purification of streptomycin and has been used in nearly every known process for the preparation of an essentially pure product. Two adsorbents, alumina and activated carbon, have been employed for column chromatography. A solution of streptomycin hydrochloride in 80% methanol-water at pH 5-6 is percolated through a vertical column packed with pretreated alumina. Eighty per cent methanol-water is fed continuously into the column until the eluate shows the presence of only a negligible quan-



tity of streptomycin. The location of the purified eluate fractions was determined at first by microbial assays, but later the Sakaguchi test (10) for guanido groups and a chloride test were employed to locate the active eluate cuts. When specific color reactions and rapid chemical assays such as the maltol assay (26) became available, the operation of the alumina columns was greatly facilitated.

According to a procedure developed by Carter and his associates (3), the alumina is first washed with dilute sulfuric acid and then with water until the washings are free from sulfate, and dried. The weight ratio of adsorbent to crude streptomycin employed for chromatography is 25:1 to 50:1. A microbiologically inactive filtrate fraction giving a positive Sakaguchi test is first observed; this is followed by a fraction giving a negative Sakaguchi test. Subsequent fractions give positive to strongly positive Sakaguchi tests, paralleling the microbiological evaluation. A small amount of active material remaining on the column is removed only by increasing the water content of the developing solution. The later eluates contain sulfate but no chloride ions, indicating an exchange of anions, streptomycin sulfate being less soluble in aqueous methanol than the hydrochloride. The most active fractions of the eluate are concentrated to remove the methanol and lyophilized to a white product, which is almost pure streptomycin sulfate.

Alumina chromatography of crude streptomycin hydrochloride has been applied successfully to the large-scale production of streptomycin. The large columns are filled with 100–200 mesh alumina and are operated under a pressure of 60 p.s.i. The performance of the chromatography is followed by spot analysis of the eluate cuts.

Since impurities such as mannosidostreptomycin, which are likely to be present in crude concentrates, do not form crystalline complexes with calcium chloride, streptomycin can also be purified by mixing a methanol solution of its hydrochloride with calcium chloride to form the crystalline streptomycin–calcium chloride complex. By proper adjustment of volumes, the complex crystallizes from the solution in high yield as elongated needles. Streptomycin hydrochloride of 40–50% purity can be used in the preparation of the complex.

**Packaging.** To ensure complete sterility in the package, the purified products are processed through additional steps for removal of spores and bacteria. This is done by passing a concentrated solution of the salts through bacterial filters; sterile techniques are employed throughout this and subsequent operations. A measured amount of solution is placed in each ampul before concentration. Removal of water from the solution is carried out by lyophilization.

When the lyophilization is carried out on trays, the product is removed from the trays, milled, and blended. These operations are all carried out under aseptic conditions. The product is then tested according to the specifications of the Food and Drug Administration; if the lot conforms to these specifications, it is subdivided into ampuls under sterile conditions in low-humidity sterile cabinets.

Since streptomycin preparations are sold and used on the basis of their free streptomycin content, vials containing the equivalent of 1 gram of free base actually contain more than this quantity of solid, for example, one gram of streptomycin base is contained in 1.19 grams of pure streptomycin hydrochloride, in 1.25 grams of pure streptomycin sulfate, and in 1.28 grams of pure streptomycin hydrochloride–calcium chloride complex. The label on the vial always indicates the weight of streptomycin base contained in the vial but does not generally state the actual weight of the contents. Unless the contents of the vial are weighed or assayed, the purity of a given sample cannot be ascertained, except for known averages.

**Market Forms.** Streptomycin powders suitable for injections are available as streptomycin sulfate and streptomycin hydrochloride-calcium chloride double salt. Mixtures of streptomycin and penicillin, suitable for systemic use, are also available. This mixture has the advantage of a wide antimicrobial spectrum. Mixtures of streptomycin and dihydrostreptomycin are available for the treatment of tuberculosis. The advantage of this mixture is a reduction in the selective toxicity of each of the two substances (see "Toxicity"). Various ointments containing combinations of streptomycin, bacitracin, and polymyxin are available for topical application.

**Stability.** Streptomycin salts containing less than 3% moisture are stable when stored at room temperature over long periods. Very little, if any, inactivation was observed when samples were held at 50°C. for 10 weeks. The expiration date for the sale of commercial streptomycin salts has been extended from 12 months to 18 months. The specifications of the Food and Drug Administration at first required that the drug be refrigerated at 15°C., but this requirement was later dropped, when the expiration date was extended.

Streptomycin solutions are stable in moderately acid and alkaline solutions, the maximum stability of culture filtrates and of aqueous and methanol solutions of streptomycin hydrochloride being in the range of pH 3.0-6.0 at temperatures below 25°C. Solutions of commercial streptomycin sulfate at pH 3-7 are stable for at least 60 days at 7-25°C. At higher temperatures, inactivation occurs; at 95°C., about 50% of the streptomycin is destroyed in 4.5 hours. Ready-to-inject solutions, usually containing 500 mg./ml., with added buffers, stabilizers, and preservatives, are stable at room temperature for at least 24 months. On aging, solutions of streptomycin and, to a lesser degree, dihydrostreptomycin tend to become darker yellow in color, but this discoloration has no effect on the therapeutic value of the product. Refrigeration delays this color change.

**Economics.** The manufacturers of streptomycin in the U.S. are: The Bristol Laboratories; Eli Lilly and Co.; Parke, Davis and Co.; Commercial Solvents Corp.; Heyden Division of American Cyanamid Co.; Abbott Laboratories; Chas. Pfizer and Co.; E. R. Squibb and Sons; Merck and Co.; and Schenley Laboratories.

Figures showing the rise in production for streptomycin and dihydrostreptomycin from 1950 to 1953 are given below (production in kilograms):

	1950	1951	1952	1953
Streptomycin	20,748	18,706	22,700	56,750
Dihydrostreptomycin	71,651	143,304	152,998	138,470

Since the introduction in 1946 of dihydrostreptomycin, its use has been growing in preference to the parent compound. This is due to the smaller number of toxic manifestations caused by the hydrogenated antibiotic.

The sales of streptomycin in 1952 in the United States were 41,000 lb. and the sales of dihydrostreptomycin were 301,000 lb. The current official sale prices of streptomycin and dihydrostreptomycin are 60¢/g. and \$2.65/5g. as the sterile powder.

### Microbiological Properties

**Antimicrobial Activity.** Streptomycin is active against a variety of Gram-positive and Gram-negative bacteria. It is also active against the mycobacteria, including the tubercle bacillus, the causative agent of tuberculosis. Streptomycin

has no activity against fungi, protozoa, rickettsiae, and viruses. The organisms sensitive to streptomycin include both animal (human) and plant pathogens (29).

The antimicrobial action of streptomycin has been described as bacteriostatic in low concentrations and as bactericidal in high concentrations. Various factors may influence the degree of bacteriostatic or bactericidal action. These are the type of test organism, the nature of the medium, the time of exposure, the pH of medium, the number of test organisms, and the temperature. A given concentration of streptomycin may be either bacteriostatic or bactericidal, depending upon the organism used and the conditions of the test.

The effectiveness of streptomycin *in vitro* for the inhibition of growth of microorganisms is usually expressed in terms of the smallest amount per milliliter of medium which completely prevents growth. These concentrations are usually referred to as bacteriostatic and furnish a basis for a comparison of the activity of streptomycin for different microorganisms. These minimal inhibiting concentrations may also indicate the effectiveness of streptomycin for the treatment of infection.

The presence of inorganic salts or glucose in the medium will reduce the bacteriostatic action of streptomycin. The addition of some substances, such as serum, stimulates growth. The pH of the medium is important, since the potency of streptomycin is a function of the pH. Maximum activity is observed at about pH 8. The activity of streptomycin is also inversely proportional to the number of organisms employed in the test and is more effective on actively growing cells. The activity of streptomycin samples is expressed in micrograms of the pure base per milligram.

**Development of Resistance.** Microorganisms exposed to any antibiotic for prolonged periods undergo marked changes in morphology and in resistance (1). The changes effected by exposure to streptomycin are more pronounced among Gram-negative than among Gram-positive organisms. Bacteria may develop resistance to streptomycin in two ways: gradually through a series of changes, or in a single step, the result of a single genetic change which produces a resistant variant. Various new types of resistant organisms may arise through spontaneous mutation, and through a process of selection.

A few colonies of streptomycin-resistant meningococci can be observed to develop from a sensitive culture when inoculated on solid media containing high concentrations of streptomycin, provided the inocula contain sufficient numbers of organisms. These colonies consist of meningococci that are highly resistant to streptomycin *in vitro* and *in vivo*, although they have developed from inocula of a sensitive strain during its initial exposure to streptomycin. Such resistant strains retain this property during prolonged subcultivation on streptomycin-free media for 1 year; there is also no change during repeated passage in untreated mice.

Strains that have acquired only slight or moderate degrees of resistance have been found to lose it readily, usually at about the same rate at which the resistance was acquired. This suggests that stability of resistant variants varies from strain to strain and also that back mutation occurs more frequently among variants possessing low degrees of resistance.

A second type of resistant colony also develops from susceptible strains during their initial exposure to streptomycin, but grows more slowly. In concentrations of streptomycin of 60 and 100  $\gamma$ /ml., these colonies differ from the previously mentioned colonies in that they are smaller and pearl-gray. Their most remarkable property is their dependence on streptomycin. Streptomycin-dependent variants grow abun-

dantly from small inocula on 100 to 400  $\gamma$ /ml. and also from heavy inocula in concentrations as low as 5  $\gamma$ /ml., but not in lower concentrations.

### Pharmacological Properties

**Absorption and Excretion.** Streptomycin passes readily into the blood stream following parenteral administration. Owing to great individual differences in absorption and excretion of the drug, significantly different blood levels are to be expected in individual patients receiving the same dosage. In general, the concentration of the drug in the blood will vary directly with the size of the individual dose and the frequency of administration.

Since 60–80% of streptomycin is excreted by the kidneys during the 24-hour period following intramuscular or intravenous injection, significant urinary levels may be obtained with comparatively small parenteral doses; these levels vary inversely with urinary output.

Significant concentrations of streptomycin have been found in the cerebrospinal fluid 24 hours after intrathecal administration of the drug with concurrent intramuscular injection at 3 hour intervals. Very little streptomycin diffuses into the spinal fluid following intramuscular or subcutaneous injection.

Streptomycin is said to pass readily from the blood into the peritoneal cavity. Following intramuscular injection, it diffuses also into the amniotic and intraocular fluids, and into the placental blood. In the absence of severe hepatic damage, it is excreted in the bile. If the cystic or hepatic duct is obstructed, no streptomycin will appear in the gall bladder. It does not diffuse readily into the pleura in most cases, nor have effective concentrations been demonstrated in the prostatic fluid following parenteral injection.

Oral administration produces no detectable concentration in blood, a negligible amount in urine, and a very high concentration in feces.

**Toxicity.** Streptomycin is a drug of low toxicity. The average  $LD_{50}$  of streptomycin in mice is 200 mg./kg. intravenously, > 700 mg./kg. subcutaneously, and 9000 mg./kg. orally. In cats the following results were obtained: 150 mg./kg. intravenously, 600 mg./kg. subcutaneously, and > 2000 mg./kg. orally. It has been administered to animals in large doses without causing serious toxic effects. Toxic signs, including dyspnea and a fall in blood pressure, may be seen after parenteral administration to animals of doses approaching the lethal level. Furthermore, when given daily over considerable periods of time, as in the treatment of tuberculosis, streptomycin has caused vestibular disturbances and, in some cases, partial loss of hearing. Streptomycin is less toxic than dihydrostreptomycin to the auditory branch of the eighth cranial nerve, and dihydrostreptomycin is less toxic to the vestibular branch of this nerve. With the small dosages and the short-term therapy required to control nontuberculous infections, such toxic manifestations are rarely a clinical problem in treatment of such diseases unless impaired renal function is present.

Allergic reactions such as drug fever, dermatitis, conjunctival irritation, and urticaria have been reported among patients, but they are infrequent, usually mild, and readily controlled by use of antihistamines. Nurses and physicians who administer streptomycin sometimes develop a contact dermatitis after handling the drug over a long period. Such reactions can be prevented by wearing rubber gloves. Persons who are allergic to streptomycin can usually tolerate dihydrostreptomycin, and vice versa.

**Administration.** The common methods of administering streptomycin and dihydrostreptomycin are intramuscularly, subcutaneously, and topically or intrathecally, intrapleurally, intraperitoneally, or by inhalation of an aerosol. The preferred method is by intermittent intramuscular injections. The gluteal, thigh, or deltoid muscles are the preferred sites. It is important to rotate the site of injection. Pain and irritation at the site of injection may be a limiting factor in use of the subcutaneous route. Intermittent intravenous administration has no advantage over the intramuscular method and, since it may produce disagreeable side reactions, this route of administration usually is avoided.

In meningitis, both intermittent intramuscular and intrathecal injections may be considered advisable. In empyema, intrapleural injections are desirable. In peritonitis, intramuscular and in some instances intraperitoneal injections are required. In bronchopulmonary infections, streptomycin has been given by nebulization.

The U.S. Food and Drug Administration suggested that streptomycin rather than dihydrostreptomycin be recommended for intrathecal therapy, except for patients allergic to streptomycin. For intrathecal and intravenous injection of streptomycin, only fresh solutions prepared from the dry powder form should be used. For intrathecal administration, the maximum amount that may safely be introduced into adults at any one time is 100 mg., smaller quantities being used at first. A solution containing 10–20 mg./ml. is commonly used. For intravenous administration, 1 or 2 grams may be dissolved in 1000 ml. of water for injection, U.S.P., or sterile isotonic sodium chloride solution for parenteral use, U.S.P., and administered at the rate of about 25 drops a minute. The concentration commonly recommended for aerosol use is 50–100 mg./ml.; for intrapleural or intraperitoneal use, 20 mg./ml.; for topical application in wet dressings or ointment form, 25–100 mg./ml.; and for oral solution, 100–200 mg./ml.

### Specifications and Assay

**Specifications.** The provisions of the Food, Drug, and Cosmetic Act require that each batch of streptomycin or of its derivative be certified by the Federal Security Administration. Each batch must have the characteristics of quality and purity established by the regulations that ensure safety and efficacy. At present, these certification regulations apply to all samples of streptomycin and dihydrostreptomycin offered for sale, even if these are pure.

From each lot, the producer submits to the Food and Drug Administration as samples five vials for every 25,000 vials of drug and one additional vial for every 5,000 vials up to a maximum of twelve vials. These samples are tested by the Food and Drug Administration and must pass tests for *potency*, which must be greater than 300  $\gamma$ /mg., measured by activity against a standard strain of *Bacillus subtilis* or *Klebsiella pneumoniae* with either the cup-diffusion method or the turbidimetric method of assay; *sterility*, tested by incubating at 37°C. for 4 days a medium containing the product and a substance known to inactivate streptomycin, such as thioglycolic acid or hydroxylamine, and then inoculating with *Klebsiella pneumoniae* one tube in test, the inoculated tube producing growth, the other tubes containing a sterile product being devoid of growth; *toxicity*, involving quantitative acute toxicity test; *histamine-like substance*, the product being tested for blood-depressor factors by intravenous injection into an anesthetized cat; *moisture*, which must not be greater

than 3.0%, as determined by drying a sample in a vacuum oven at 60°C. at a pressure of 5 mm. or less of mercury for 3 hours; *pH*, an aqueous solution of 0.2 gram base per milliliter having a pH of 4.5-7.0; *solubility*, solutions prepared by adding 0.2 gram of streptomycin base to 1 ml. of water, to 5% dextrose solution, or to physiological saline solution being free from turbidity or undissolved material; *pyrogens*, no positive pyrogen reaction being obtained when 10 mg. of streptomycin base per milliliter is injected into rabbits. If the samples meet the established specifications, the lot of streptomycin is certified for sale.

**Assay.** Both biological and chemical methods are used for determining the potency of streptomycin. The biological methods can be subdivided into three broad groups.

The *agar-plate diffusion method* has been most commonly used, although its sensitivity and reproducibility are not quite so satisfactory as those of the turbidimetric method. Because of differences inherent in the mode of action, in physical characteristics, and in effects of culture media on streptomycin, the method is somewhat less accurate than the comparable one for penicillin. The choice of test organism is important. Usually a strain of *Bacillus subtilis* (American Type Culture Collection 6633) is used in the official tests employed by the Food and Drug Administration in the certification of streptomycin.

For the *turbidimetric method*, any sensitive organism such as nonencapsulated *Klebsiella pneumoniae* can be used, provided it grows rapidly, and the degree of turbidity can be correlated with the concentration of streptomycin. This method is used by the Food and Drug Administration in its streptomycin certification program (5).

The *serial-dilution method* (the inhibition of sensitive organisms by various dilutions of streptomycin) is the simplest method and is widely used in determining concentrations of streptomycin in broths and in body fluids. In this method *Klebsiella pneumoniae* is used.

The chemical methods depend on: (1) formation of an easily identified substance, maltol by alkaline hydrolysis and (2) formation of identifiable complexes by interaction of the streptose aldehydic group of streptomycin with appropriate carbonyl group reagents (10,17,20).

### Uses

Streptomycin and dihydrostreptomycin are effective against diseases caused by many mycobacteria and most Gram-negative and many Gram-positive bacteria.

The chief indications for the use of streptomycin alone or streptomycin in combination with other chemotherapeutic agents are: tuberculosis, bacteremia, meningitis, and urinary tract infections due to streptomycin-sensitive strains of various Gram-negative bacteria; *Hemophilus influenzae* infections of the blood stream and heart, meninges, and respiratory and urinary tracts; endocarditis due to penicillin-resistant organisms; pneumonia due to *Klebsiella pneumoniae*; empyema and other pulmonary infections due to streptomycin-sensitive organisms; chancreoid; granuloma inguinale; gonorrhea unresponsive to penicillin; brucellosis; tularemia; plague; glanders; corneal ulcers caused by *Pseudomonas aeruginosa*; wounds and cutaneous infections due to *Proteus vulgaris*; peritonitis and enteritis; and prophylactically in gastrointestinal surgery (13).

An etiologic diagnosis is advisable, when practicable, to provide a guide to the

dose of streptomycin and the duration of treatment. In the treatment of some infections, different dosage schedules and different routes of administration give better results (see p. 77).

In mixed infections caused by Gram-positive and Gram-negative organisms, a combination of streptomycin and other antibiotics or of streptomycin and sulfa drugs (*q.v.*) may be necessary. It is especially advisable, therefore, that these cases be studied etiologically if possible.

The treatment of tuberculosis with streptomycin has been undergoing considerable change since its usefulness was first demonstrated. Streptomycin is a highly effective agent in the treatment of many forms of tuberculosis. Its therapeutic value is limited by the fact that after exposure to streptomycin for weeks or months, strains of *Mycobacterium tuberculosis* resistant to the effects of the drug may be isolated. Therefore, streptomycin is used only as an adjunct to other measures in the treatment of tuberculosis and is primarily of value in conditions in which temporary suppression of the infection will enable the patient to gain ascendancy over the disease; healing then occurs by natural process. Streptomycin should not be used in minimal and primary pulmonary tuberculosis, which will respond readily to routine treatment, since there is the danger that resistant organisms will emerge. Unnecessary use of the drug may interfere with its effectiveness when there is a more serious need.

In pulmonary tuberculosis streptomycin is used mainly in combination with *p*-aminosalicylic acid (PAS) (see Vol. 12, p. 57) and isoniazid (INH) (see also *Tuberculostatics*). The usual dosages are (1) 1 gram streptomycin a day + 12 grams PAS daily; (2) 1 gram of streptomycin twice a week + 12 grams PAS daily; (3) 1 gram streptomycin daily + 300 milligrams INH daily (18). It is now common practice to use a mixture of streptomycin and dihydrostreptomycin in place of streptomycin alone. In this manner the toxic effect of each substance is minimized (see p. 76).

Other types of tuberculosis that have responded to treatment with streptomycin include exudative pulmonary disease, ulcerating lesions of the respiratory tract, and tuberculous draining sinuses. It has some place in the treatment of bilateral renal tuberculosis or tuberculosis of a solitary kidney. It also is used before and after thoracic surgery for pulmonary tuberculosis.

Oral administration of streptomycin is useful in preparing patients for surgical operations on the large intestine and in treating gastrointestinal infections. It is one of the safest antibiotics for gastrointestinal therapy because it is not absorbed into the blood and therefore can have no toxic effect on the patient. Moreover, it does not destroy the entire bacterial flora of the intestine and therefore does not have the untoward effects often met with in use of certain other antibiotics.

The clinician may occasionally find it desirable to apply streptomycin locally for the treatment of wounds infected by organisms susceptible to the action of the antibiotic. Satisfactory solutions for local use vary in concentration from 0.25 to 100 mg./ml.

In recent years, therapeutic application of mixtures of streptomycin and other antibiotics and sulfa drugs has been reflected in an increasing number of favorable clinical reports. Such combined therapy has proved of value in the treatment of endocarditis and bacteremia, surgical infections including peritonitis and extensive burns, gynecologic or obstetric infections, and other infections of many types.

Streptomycin is also used in veterinary medicine (12,25). Although antibiotics are not much used in phytopathology, streptomycin in early experiments proved one of the most promising in the treatment of plant bacterial infections (19,35).

Like many other antibiotics, streptomycin seems to have a certain growth-promoting action in animals. This action is not so striking as the response to penicillin, chlortetracycline, and bacitracin. At least one animal feed supplement on the market contains streptomycin (32).

### Related Compound

**Hydroxystreptomycin** ( $C_{21}H_{39}N_7O_{13}$ , IV) is produced by various species of *Streptomyces* including a variant of *S. rurireticuli* (formerly *S. reticuli*). It is an organic base, very soluble in water, less soluble in lower alcohols, and insoluble in other organic solvents. Hydroxystreptomycin hydrochloride showed a specific rotation in water of  $-91^\circ$ . It is like streptomycin in that it is stable in weak acid and weak base solutions at room temperature. On alkaline hydrolysis it yields pyromeconic acid (3-hydroxy-4H-pyrone,  $O.CH:COH.CO.CH:CH$ ) and isokoic acid.

Hydroxystreptomycin is active against Gram-positive, Gram-negative, and acid-fast organisms. Its  $LD_{50}$  for subcutaneous injection in white mice is 865 mg./kg. The toxic properties of hydroxystreptomycin and its derivative dihydroxystreptomycin are essentially those of streptomycin and dihydrostreptomycin respectively (1).

### Bibliography for Streptomycin

- (1) Braun, W., *Bacterial Genetics*, Saunders, Philadelphia, 1953.
- (2) Brink, N. G., Kuehl, F. A., Jr., and Folkers, K., *Science*, **102**, 506-07 (1945).
- (3) Carter, H. E., Clark, R. K., Jr., Dickman, S. R., Loo, Y. H., Skell, P. S., and Strong, W. A., *J. Biol. Chem.*, **160**, 337 (1945).
- (4) Dulaney, E. L., *Mycologia*, **45**, 481-87 (1953).
- (5) *Federal Register*, **12**, No. 67, 2225 (1947).
- (6) Feldman, W. H., and Hinshaw, H. C., *Proc. Staff Meetings Mayo Clinic*, **19**, 593-99 (1944).
- (7) Fried, J., and Titus, E., *J. Biol. Chem.*, **168**, 391-93 (1947).
- (8) Hinshaw, H. C., Feldman, W. H., and Pfuetze, K. H., *Am. Rev. Tuberc.*, **54**, 191-203 (1946).
- (9) Hooper, I. R., and Kaplan, M. A., *J. Am. Chem. Soc.*, **75**, 6055 (1953).
- (10) Kanazawa, Y., *J. Antibiotics (Japan)*, **4**, 552-53 (1951).
- (11) Keefer, C. S., Blake, F. G., Lockwood, J. S., Long, P. H., Marshall, E. K., and Wood, W. B., *J. Am. Med. Assoc.*, **132**, 4-10, 70-77 (1946).
- (12) Kellberg, J. E., *Vet. Med.*, **42**, 220-22 (1947).
- (13) Kitchen, H. B., and Waksman, S. A., *J. Am. Pharm. Assoc., Sci. Ed.*, **42**, 522-36 (1953).
- (14) Kuehl, F. A., Jr., Flynn, E. H., Brink, N. G., and Folkers, K., *J. Am. Chem. Soc.*, **68**, 2096-99 (1946).
- (15) Kuehl, F. A., Jr., Peck, R. L., Hoffhine, C. E., Jr., Graber, R. P., and Folkers, K., *J. Am. Chem. Soc.*, **68**, 1460 (1946).
- (16) Lemieux, R. V., and Wolfrom, M. L., *Advances in Carbohydrate Chemistry*, Academic Press, N.Y., 1948, Vol. III, pp. 337-84.
- (17) Marshall, E. K., Blanchard, K. C., and Buhle, E. L., *J. Pharm. Exptl. Therap.*, **90**, 367-74 (1947).
- (18) Minutes of the Veterans Administration Meetings on the Chemotherapy of Tuberculosis, Conferences 11 to 13 (1952, 1953, 1954).
- (19) Mitchell, J. W., Zaunmeyer, W. J., and Preston, W. H., *Phytopathology*, **44**, 25-29 (1954).
- (20) Monastero, F. A., *J. Am. Pharm. Assoc., Sci. Ed.*, **41**, 322-24 (1952).
- (21) Peck, R. L., Hoffhine, C. E., and Folkers, K., *J. Am. Chem. Soc.*, **68**, 1390-91 (1946).
- (22) Pruner, D., and Starkey, R. L., *Science*, **113**, 127 (1951).
- (23) Prescott, S. C., and Dunn, C. G., *Industrial Microbiology*, McGraw-Hill, N.Y., 1949.



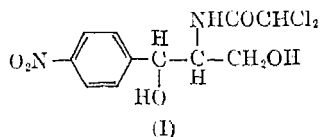
- (24) Schatz, A., Bugie, E., and Waksman, S. A., *Proc. Soc. Exptl. Biol. Med.*, **55**, 66 (1944).
- (25) Scheidy, S. F., *J. Am. Vet. Med. Assoc.*, **118**, 213-20 (1951).
- (26) Schenck, J. R., and Spielman, M. A., *J. Am. Chem. Soc.*, **67**, 2276-77 (1945).
- (27) Tanaka, M., Yonehara, H., Sado, T., and Sumiki, Y., *J. Antibiotics (Japan)*, **4**, Suppl. A., 20-22 (1951).
- (28) Titus, E., and Fried, J., *J. Biol. Chem.*, **168**, 393-94 (1947).
- (29) Waksman, S. A., *Streptomycin, Its Nature and Practical Application*, Williams and Wilkins, Baltimore, 1949.
- (30) Waksman, S. A., *The Literature on Streptomycin*, Rutgers University Press, New Brunswick, N.J., 1st ed., 1948, 2nd ed., 1952.
- (31) Waksman, S. A., and Schatz, A., *Proc. Natl. Acad. Sci.*, **31**, 208-14 (1945).
- (32) Welch, H., *Antibiotics & Chemotherapy*, **4**, 89 (1954).
- (33) Woodruff, H. B., Nunheimer, T. D., and Lee, S. B., *J. Bacteriol.*, **54**, 535-541 (1947).
- (34) Woodruff, H. B., and Ruger, H., *J. Bacteriol.*, **56**, 315 (1948).
- (35) Zaumeyer, W. J., Thomas, H. R., Mitchel, J. W., and Fisher, H. H., *Phytopathology*, **43**, 407 (1953).
- (36) U.S. Pat. 2,516,682 (July 25, 1950), R. Donovan, W. L. Koerber, and W. C. Rake (to E. R. Squibb & Sons).
- (37) U.S. Pat. 2,538,943 (Jan. 23, 1951), L. E. McDaniel and D. Hendlin (to Merck & Co.).
- (38) U.S. Pat. 2,540,238 (Feb. 6, 1951), W. A. Bittenbender and R. D. Babson (to Merck & Co.).
- (39) U.S. Pat. 2,541,420 (Feb. 13, 1951), E. E. Howe and J. Putter (to Merck & Co.).
- (40) U.S. Pat. 2,541,726 (Feb. 13, 1951), P. Trussell (to Ayerst, McKenna, and Harrison, Ltd.).

SELMAN A. WAKSMAN AND H. A. LECHEVALIER

### CHLORAMPHENICOL

Chloramphenicol, U.S.P. XIV, N.N.R. (Chloromycetin) (I) formula weight 323, the first of the so-called "broad-spectrum" antibiotics (1947), was originally isolated from cultures of *Streptomyces venezuelae* (5,28). It is a neutral substance with a bitter taste and is moderately soluble in water and freely soluble in many organic solvents. The antibiotic was made available in crystalline form from the start for investigative and clinical use and is the only antibiotic drug for which synthetic methods of production have proved feasible commercially. It is commercially available as the free compound and as its palmitate and stearate.

Chloramphenicol was found to inhibit many Gram-positive and Gram-negative bacilli and cocci, some spirochetes, several rickettsiae, and certain of the larger viruses. Chloramphenicol was the first substance found active both in the laboratory and in human patients against typhus fever and other rickettsial infections and is still the only regularly effective agent for typhoid fever.



### Physical and Chemical Properties

Crystalline chloramphenicol occurs as colorless needles or elongated plates, m.p. 150.5-51.5°C.,  $[\alpha]_D^{25} +19^\circ$  (5% in absolute ethyl alcohol) and  $-25.5^\circ$  (5% in ethyl acetate). It is soluble at 25°C. to the extent of 2.5 mg./ml. in water and 150.8 mg./ml. in propylene glycol. It is very soluble in methanol, ethyl alcohol, *n*-butyl

alcohol, acetone, ethyl and amyl acetate, and *N,N*-dimethylacetamide; fairly soluble in diethyl ether; and insoluble in benzene and petroleum ether. Although chloramphenicol is a nonionic compound, solutions are faintly acid: pH 5.5 in water, pH 5.2–5.0 in propylene glycol, and pH 4.7 in 50% aqueous dimethylacetamide (1,2,10). Chloramphenicol has a characteristic ultraviolet absorption spectrum. In neutral and acidic solutions, there is a relatively broad band with a peak at 278 m $\mu$ , a minimum at 237 m $\mu$ , and a second partially resolved band at 215 m $\mu$ . The extinction coefficient,  $E_{1\text{ cm.}}^{1\%}$ , is 298 at 278 m $\mu$  in water, and 312 at 274 m $\mu$  in ethyl alcohol. Its infrared absorption spectrum, determined as a Nujol mull, is characterized by a number of important bands, the 12 strongest being at 2.97, 3.05, 5.93, 6.40, 6.58, 7.41, 8.02, 9.02, 9.36, 10.26, 11.80, and 12.22  $\mu$ , respectively.

Physical data, tests for functional groups, degradation experiments, and synthesis have established the structure as D(–)-*threo*-2-dichloroacetamido-1-*p*-nitrophenyl-1,3-propanediol (D(–)-*threo*-2,2-dichloro-*N*-[ $\beta$ -hydroxy- $\alpha$ -(hydroxymethyl)-*p*-nitrophenethyl]acetamide) (C.A.) (26). The molecule may be considered as comprising two parts, the 2-acylamidopropanediol side chain containing two asymmetric carbon atoms, and the *p*-nitrophenyl group. Of the four possible stereoisomers, only the D-*threo* is active against microorganisms. The stereochemical configuration of the side chain is thus specific in conferring antimicrobial properties. The aromatic part of the molecule is less specific for antimicrobial activity, as shown by the moderate activity of analogs in which the nitro group is replaced by iodine or by the methylsulfonyl group.

Esterification of one of the hydroxyl groups of the propanediol side chain with palmitic acid readily yields *chloramphenicol palmitate*,  $[\alpha]_D^{25}$  24.6° (5% in absolute ethyl alcohol),  $E_{1\text{ cm.}}^{1\%}$  179 at 271 m $\mu$  in ethyl alcohol (7), a white crystalline substance which is only slightly soluble in water and petroleum ether but freely soluble in ethyl alcohol, chloroform, ether, and benzene. The palmitate shows no significant antimicrobial activity *in vitro* but becomes hydrolyzed in the duodenum to active chloramphenicol. The ester is tasteless and in suspension provides an oral dosage form of the antibiotic acceptable to those unable to take capsules. Other esters have also been prepared (36).

### Preparation and Manufacture

Chloramphenicol was originally prepared and later manufactured by a biochemical process but is now largely produced by synthesis.

**Biochemical Process.** Various strains of the actinomycete *Streptomyces venezuelae* (6) (*S. phaeochromogenus* var. *chloromyceticus* (19,23)) or the related species *S. omiyaensis* (33) are cultivated under submerged aerated conditions in complex nutrient broth media containing glucose, maltose, starch, or glycerol; sodium nitrate, amino acids, or undefined organic nitrogen compounds; and inorganic salts (10,11, 30,31,32,35). Potencies of 200–275  $\gamma$ /ml. have been reported for shaken flask cultures in a synthetic medium containing (in per cent) glycerol 3.0, DL-phenylalanine 0.02, L-tyrosine 0.02, DL-methionine 0.01, sodium nitrate 0.2, dipotassium phosphate 0.1, magnesium phosphate heptahydrate 0.05, potassium chloride 0.05, and sodium chloride 1.0. A medium containing (in per cent) starch 2.0, peptone 0.5, meat extract 1.0, dipotassium phosphate 0.1, and sodium chloride 1.0 reached similar potency, and when this medium was supplemented with the above-named amino acids the potency was doubled (35). With a different strain of organism and a medium con-

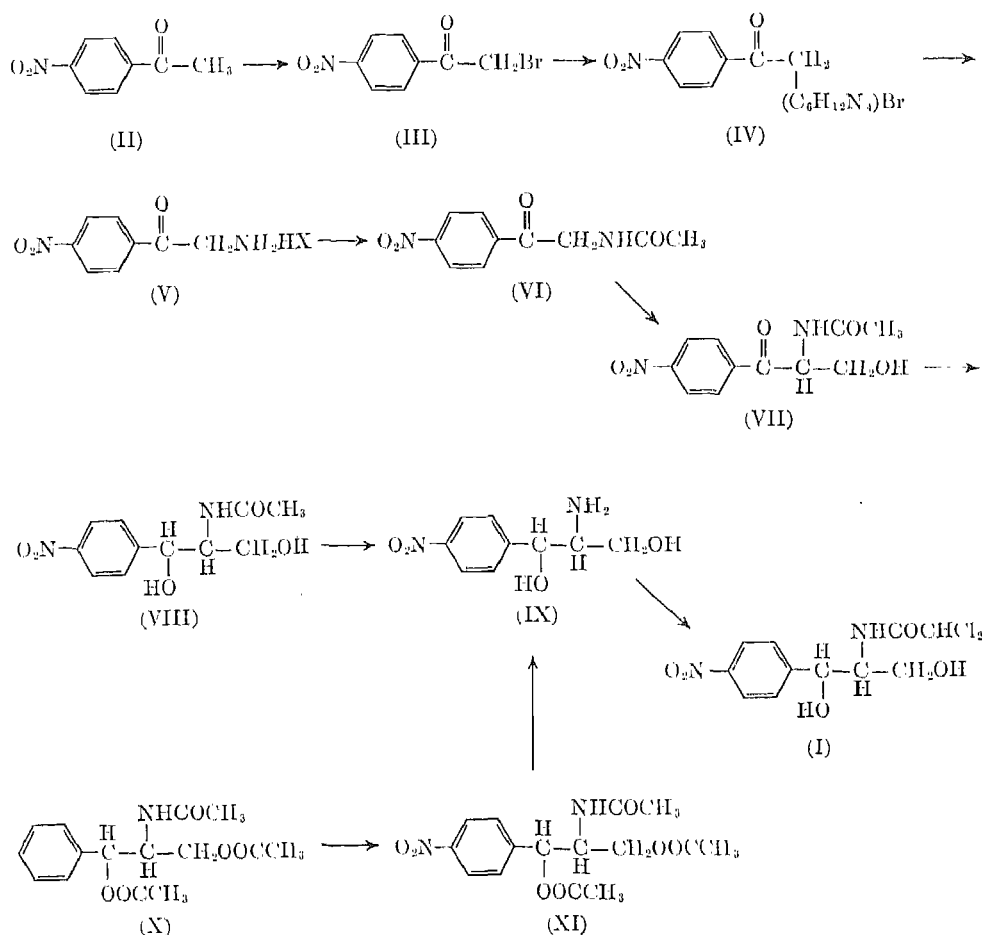
taining (in per cent) starch 4.0, peptone 1.0, sodium nitrate 0.4, dipotassium phosphate 0.2, potassium chloride 0.1, magnesium chloride heptahydrate 0.1, and ferrous sulfate 0.002, potencies of 300–400  $\gamma$ /ml. were attained in shaken flasks and 400–650  $\gamma$ /ml. in fermentation tanks (22).

Commercial production was reported in 1949 (24) to employ a pH 7 fermentation medium containing glycerol, wheat gluten, sodium carbonate, and sodium chloride. The contents of a 50-gal. fermentor, inoculated with spores, is used after approximately 24 hours at 86°F. to sow a 500-gal. fermentor which after another 24 hours at 86°F. provides the volume of seed required for a 5000-gal. fermentor where growth is allowed to proceed for approximately 3 days at 82°F. Asepsis is maintained by the usual precautions throughout the fermentation (see also *Sterilization*). Aerobic conditions are provided by air from a carbon-ring reciprocating duplex compressor, which is sterilized by passage through a carbon column and is distributed through a perforated ring sparger centrally located at the bottom of each fermentor. Mechanical agitation is induced by turbine impellers mounted on a centrally located top-entering shaft, together with peripheral vertical baffles. The temperature is closely controlled by circulating cold water through jackets or internal coils. Provision is made for foam control, pH determination, and aseptic sampling.

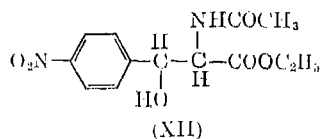
The fermented broth is clarified by passage through a pressure-type rotary precoat filter, and the active material is removed with a centrifugal countercurrent extractor into amyl acetate. The extract is concentrated in a natural-circulation vacuum evaporator and washed with dilute sulfuric acid, sodium bicarbonate, and deionized water. After further concentration in a small glass vacuum still and cooling to 8°C., crystallization occurs. The crude crystals are manually filtered, vacuum-dried, and dissolved in hot water. The hot solution is decolorized by carbon treatment, clarified by filtration, and cooled to induce crystallization. The purified crystals are filtered, washed with deionized water, dried, pulverized, and sieved. The chloramphenicol is then ready for pharmaceutical use (21,24). The biochemical process yields a single optical entity having the *D-threo* configuration.

**Synthesis.** The most generally used process of synthesis (24) starts from *p*-nitroacetophenone (17,18) but acetophenone may be used alternatively. The various steps are shown in Scheme 1. The bromination (II  $\rightarrow$  III) can be carried out in a variety of inert solvents, yield > 90%. The formation of a hexamethylenetetramine complex (IV) is usually carried out in a chlorinated solvent and followed by an alcoholic mineral acid hydrolysis to obtain the corresponding mineral acid salt (V). Acetylation of (V) is carried out in cold water with acetic anhydride and mild alkali, overall yield, (III  $\rightarrow$  VI), 67%. The addition of formaldehyde to (VI) occurs in the presence of sodium bicarbonate, yield 86%. The Meerwein-Ponndorf reduction of (VII) to (VIII) yields almost exclusively the *DL-threo* racemate in 41% yield. (If acetophenone is used as starting material, the hydroxyl groups of the compound analogous to (VIII) are protected by acetylation and the triacetyl derivative (X) is nitrated with fuming nitric acid to give (XI).) Acid hydrolysis of either (VIII) or (XI) yields the racemic base (IX), which is resolved into its optical antipodes by crystallization of its salt with an optically active acid, for example, tartaric acid (*q.v.*) in methanol. After recovery of the optically active *D*-base by precipitation with alkali, 30% yield, main crop, the dried base may be acylated by a variety of agents, the most commonly used being methyl dichloroacetate, to give a 95% yield of chloramphenicol (I). The overall yield is about 6% of theory.

SCHEME 1



A number of alternative routes fitting into this scheme have been worked at least on a laboratory scale. Thus the free amino diol corresponding to (X) has been obtained by reduction of 1-phenyl-2-nitro-1,3-propanediol as a separable mixture of *DL-threo* and *DL-erythro* racemates (3). The *DL-threo* racemate of (VIII) (or the un-nitrated analog) has been obtained by lithium aluminum hydride reduction of the corresponding  $\beta$ -phenylserine ester (XII) (14).



With the introduction of synthetic methods, the question of optical isomer purity arose, since it may be assumed that the fermentation material would contain none of the levorotatory (in alcohol) isomer. Using specific rotation methods of analysis, the reading error will be 1% (for example,  $\pm 0.02^\circ$  on a  $1.90^\circ$  reading, 5% in absolute ethyl alcohol, 2-dm. tube) at best. Thus, under optimum conditions, presence of

the inactive isomer could be detected at  $> \pm 1\%$ , assuming an excellent operator and absence of any extraneous nonrotatory impurity. It was found that the racemic compound (I) can be determined in the presence of either optical antipode by x-ray powder diagram using the diffraction line at  $8.5^\circ$  ( $2\theta$ ). The sensitivity of this determination is such that the presence of less than  $1\%$  of the bacteriologically inactive form can be detected in the crystalline, active antibiotic.

**Market Forms.** Chloramphenicol is marketed for use in human and veterinary medicine in product forms suitable for oral, rectal, parenteral, and topical administration. Oral product forms include capsules and tablets containing chloramphenicol with or without inert diluents and binding substances, an aromatic flavored powder for mixing with beverages, and a palatably flavored suspension of the palmitate or stearate ester of chloramphenicol. A capsule containing chloramphenicol and streptomycin or dihydrostreptomycin is also marketed. Suppositories and punctured capsules are administered rectally. Parenteral product forms include the sterile powder in ampuls for reconstitution with *N,N*-dimethylacetamide and further aqueous dilution for intravenous administration, and in rubber-diaphragm-stoppered, aluminum-capped vials for aqueous suspension and intramuscular injection. Topical product forms include chloramphenicol solutions in propylene glycol with benzocaine for use in the external ear and on the skin (also a methanol solution used in Australia and New Zealand for treatment of sheep foot rot), eye drops, dusting powder and impregnated gauze for wound dressing, sterile powder with borate buffer to be dissolved in water for ophthalmic use, and creamy ointments for dermal, ophthalmic, and bovine intramammary application. The price of chloramphenicol is competitive with that of other broad-spectrum antibiotics.

**Stability.** Chloramphenicol solutions, when exposed to sunlight, to an ultraviolet source, or to high temperature, decompose with formation of hydrochloric and dichloroacetic acids and tarry material after a few hours (13a). The dry solid is stable at room temperatures in ordinary diffuse light for at least 5 years. Sterile aqueous solutions held at  $100^\circ\text{C}$ . retain their antimicrobial activity  $> 5$  hours but lose approximately half their activity if heated at  $100^\circ\text{C}$ . for approximately 16 hours. At  $37^\circ\text{C}$ ., activity remains practically unimpaired for a month but deteriorates slowly thereafter, dropping to approximately half after 6 months, to 25–30% after one year, and to about 10% after 2 years. At room temperature (about  $25^\circ\text{C}$ .) sterile aqueous solutions protected from light are stable for 3–6 months and lose approximately half their activity over a 2-year period. At  $5^\circ\text{C}$ . there is little or no loss in activity of aqueous solutions for at least 2 years. Chloramphenicol is also relatively pH-stable; aqueous solutions adjusted to levels between pH 0.4 and pH 9.5 retain their activity at  $25^\circ\text{C}$ . for at least 24 hours but those above pH 10 do not.

### Microbiological Properties

**Antimicrobial Spectrum.** Chloramphenicol is classed as a broad-spectrum antibiotic because it exerts marked inhibitory activity toward Gram-positive and Gram-negative cocci and bacilli, spirochetes, actinomycetes, rickettsiae, and the larger viruses (20). It is relatively inactive, however, against protozoa and other animal parasites, fungi, and the smaller viruses.

**Development of Resistance.** Populations of some strains of bacteria exposed for many generations to chloramphenicol exhibit a gradually increasing resistance to

the inhibitory action of the antibiotic. Such populations are sometimes found to be more resistant than they initially were to the tetracyclines as well, but usually not so to bacitracin, neomycin, penicillin, and streptomycin. Increased resistance to chloramphenicol is often reversible in whole or in part when the organism grows in the absence of the antibiotic. Despite the increasing incidence of infections with staphylococci resistant to various antibiotics, strains resistant to chloramphenicol are rarely encountered.

### Pharmacological Properties

**Absorption and Excretion.** Following oral administration, chloramphenicol is rapidly absorbed from the gastrointestinal tract and widely distributed to body fluids and tissues. In human beings receiving chloramphenicol by mouth, blood levels of the drug reach a maximum in 2-4 hours and gradually return to zero in 18-24 hours. These levels are roughly proportional to the size of the dose; in a group of adult males, for example, peak serum levels averaged 4  $\gamma$ /ml. after a single 0.5 gram oral dose, 9  $\gamma$  after 1.0 gram, and 14  $\gamma$  after 2.0 grams (16). Higher levels are reached on repeated administration of the drug. Comparison of chemical and microbiological assays on blood serum reveal only slightly greater values for total nitro compounds, indicating that most of the drug in the blood is in the form of unchanged antibiotic.

The kidneys and liver of dogs, mice, rats, and guinea pigs generally show the highest concentrations of nitro compounds—a situation reflecting the utilization of these organs as routes of excretion for chloramphenicol metabolites in these animals. The lungs, spleen, heart, and skeletal muscle attain concentrations of nitro compounds similar to those found in blood. Brain and human spinal fluid show substantial but lower chloramphenicol concentrations than blood, while human urine levels exceed blood serum levels more than tenfold. Chloramphenicol is also found in pleural and ascitic fluids, in human milk, and in the cord blood of newborn infants.

Humans excrete most of the drug in the urine as a highly water-soluble conjugate with glucuronic acid, representing over 80% of the dose in a 24-hour period; approximately 5% of the dose appears in the urine as unchanged antibiotic. Small amounts of a third nitro compound are also found in human urine, representing a hydrolysis product of chloramphenicol in which the dichloroacetic acid portion has been removed. The glucuronide conjugate recovered from urine can be hydrolyzed *in vitro* by bacterial action and by the enzyme  $\beta$ -glucuronidase to regenerate free chloramphenicol. In the rat and dog, large amounts of the glucuronide are excreted in the bile; active chloramphenicol is regenerated by bacterial action in the intestinal tract, with subsequent reabsorption of a portion of the antibiotic. In addition, aromatic amines may be formed by bacterial reduction of the nitro group in the intestinal tract of some lower animals. This process is insignificant in humans because the primary route of excretion is in the urine. Nevertheless, the relatively small amounts of chloramphenicol excreted in human bile reach concentrations high enough to exert antibacterial effects (9,34).

**Toxicity.** Chloramphenicol is a relatively nontoxic substance. The maximum tolerated single intravenous dose (LD<sub>50</sub>) in milligrams per kilogram is 75 (in propylene glycol) for rabbits, 125 (in water) for albino mice, 150 (in propylene glycol) for dogs, and 200-225 (in dimethylacetamide) for albino rats. Considerably higher doses are tolerated orally: > 300 mg./kg. by dogs, 1500 by albino mice, and 3000 by rabbits.

No cumulative toxic effect has been observed in dogs on oral daily divided dosage of 200 mg./kg., 5 days a week, for over 18 months. Albino mice tolerate 425 mg./kg. per day orally for 4 weeks. Rabbits have tolerated 1 gram/kg. per day, 5 days a week, for 12 weeks, and albino rats have been found to tolerate 1% in the diet for over a year without evidence of cumulative toxic effects (12,26a,34b).

In humans, therapeutic doses of chloramphenicol are generally well tolerated. Nausea and vomiting occur infrequently, as does looseness of stool which is often overcome by concurrent administration of B-complex vitamins. Sensitivity reactions, such as skin rash and wheal, are rare; pruritis develops only occasionally, sometimes associated with multiplication of *Candida albicans* (34). While the incidence of blood dyscrasias associated with chloramphenicol therapy is uncommon, cases of serious disorders including aplastic anemia have been reported. Although definitive proof of a causal relationship is lacking, such possibilities should be recognized. The use of chloramphenicol should be reserved for patients with specific infections due to microorganisms known to be sensitive to concentrations of chloramphenicol attainable. Adequate hematologic control is advised (15a,34a).

#### Specifications and Assay

**Specifications.** Chloramphenicol is certified as an antibiotic by the Food and Drug Administration of the U.S. Department of Health, Education, and Welfare (6a). The U.S.P. specifies 97–103%  $C_{11}H_{12}Cl_2N_2O_5$  and compliance with F.D.A. requirements. The U.S.P. also includes description, solubility, melting range, specific rotation in absolute ethyl alcohol, identification by a colorimetric test for the nitro group and the U.S.P. test for chloride, and assay by spectrophotometric test of an aqueous solution. The Food and Drug Administration specifies test methods and requirements for the antibiotic itself and for the various product (market) forms.

Certification by the F.D.A. requires potency of not less than 900  $\gamma$ /mg. for chloramphenicol, 555  $\gamma$ /mg. for the palmitate, and 85% of labeled potency for product forms. Potency is assayed (1) by a microbiological cylinder-plate method employing *Sarcina lutea* or (2) by a spectrophotometric test of an absolute ethyl alcohol solution. Chloramphenicol and its product forms may be assayed by method (1) (above); the palmitate and its suspension are assayed by method (2); chloramphenicol, its capsules, and aqueous solution for injection may also be assayed by method (2).

For F.D.A. certification, chloramphenicol batches must also be (1) sterile, (2) nontoxic, (3) nonpyrogenic, and (4) free of histamine. They should also display the constants: m.p.  $151^\circ C. \pm 2^\circ$ ; pH 4.5–7.5 ( $H_2O$ );  $[\alpha]_D^{20} + 20^\circ \pm 1.5^\circ$  (absolute ethyl alcohol),  $[\alpha]_D^{25} + 18.5^\circ \pm 1.5^\circ$  (5% in absolute ethyl alcohol); and  $E_{1\%}^{1\text{cm.}} 298 \pm 9$  at 278  $m\mu$  ( $H_2O$ ). Specifications (1), (3), and (4) are not required of batches to be used in product forms intended for oral or topical administration. Batches of the palmitate must melt at  $89^\circ C. \pm 3^\circ$  and have an extinction coefficient of  $178 \pm 6$  at 271  $m\mu$  in absolute ethyl alcohol.

**Assay. Microbiological Methods.** Solutions of chloramphenicol in water or body fluids can be assayed by a turbidimetric method (15). This method can be used with various sensitive organisms, notably *Shigella sonnei* (American Type Culture Collection 11060). The light transmission of broth cultures of the organism containing graded concentrations of the antibiotic is the basis for the standard curve used in the assay of unknown samples. This method requires an incubation period of 3.5–4 hours, is sensitive to as little as 1.0  $\gamma$ /ml., and has a precision of considerably less than  $\pm 10\%$ .

A manometric procedure has also been employed, based upon inhibition of oxygen uptake by *Escherichia coli* in the presence of chloramphenicol (13b). The chloramphenicol titer of body fluids and tissue extracts containing at least 2.0  $\gamma$ /ml. can also be estimated by a cylinder-plate agar diffusion method, employing a sensitive strain of *Bacillus subtilis* (29). More concentrated solutions can be diluted to approximately 50  $\gamma$ /ml. and assayed by a similar method employing *Sarcina lutea* (25). Other methods have been described, among them those in which solutions of the antibiotic are brought in contact with the entire exposed surface of the seeded agar in tubes of small diameter or in cups or wells cut into a thin layer of seeded agar in plates, and the zone of growth inhibition measured.

**Physical Methods.** In the absence of interfering materials, chloramphenicol is conveniently assayed by the ultraviolet spectrophotometer, with calculations based on the absorption constants given under "Physical and chemical properties." A polarographic method has also been described (13).

**Chemical Methods.** Chloramphenicol can also be determined by a colorimetric procedure based on the reduction of the aromatic nitro group to a primary amine with titanous chloride or metallic zinc, followed by diazotization and coupling with the Bratton-Marshall reagent, *N*-(1-naphthyl)ethylenediamine dihydrochloride. This determination, when applied to body fluids, includes certain inactive metabolic derivatives of chloramphenicol which still retain the nitro group, but it can be made specific by preliminary extraction with organic solvents (8).

### Uses

Chloramphenicol is used for treating a wide range of infectious diseases of humans (34) and animals (4,27). Human infections responsive to treatment with chloramphenicol include the rickettsial fevers—epidemic, scrub, and endemic typhus, Rocky Mountain spotted fever, rickettsialpox, and Q fever; typhoid and other enteric fevers including bacillary dysenteries; urinary tract infections; pertussis and *H. influenzae* infections; laryngotracheobronchitis; bacterial pneumonias; undulant fever; and a variety of miscellaneous clinical entities that include surgical and blood-stream infections, tularemia, ulcerative colitis, gonorrhea, syphilis, granuloma inguinale, lymphogranuloma venereum, primary atypical pneumonia, psittacosis, trachoma, Boutonneuse fever, and Carrion's disease.

In veterinary medicine, chloramphenicol is used to treat many common infections of both large and small animals. Responsive diseases of small animals include gastroenteritis of dogs with accompanying diarrhea, certain urinary tract infections, secondary bacterial invaders of canine distemper, infectious feline panleukopenia, infectious pneumonitis of kittens, tonsillitis, infectious bronchitis, pneumonia, and the secondary bacterial invaders associated with infectious hepatitis. Diseases of large animals amenable to chloramphenicol therapy include infectious diarrhea of calves, colts, and lambs, hemorrhagic septicemia of calves, calf pneumonia, calf diphtheria, swine enteritis, metritis, and certain of the infections found following retained placenta. Infectious keratitis, some cases of bovine mastitis, and foot rot of sheep (in Australia and New Zealand) are often brought under control by local application of chloramphenicol.

### Bibliography for Chloramphenicol

- (1) Bartz, Q. R., *J. Biol. Chem.*, **172**, 445-50 (1948).
- (2) Carter, H. E., Gottlieb, D., and Anderson, H. W., *Science*, **107**, 113 (1948).
- (3) Controulis, J., Rebstock, M. C., and Crooks, H. M., Jr., *J. Am. Chem. Soc.*, **71**, 2463-68 (1949).



- (4) Eastman, J. W., Schlingman, A. S., Manning, M. C., and Eads, F. E., *J. Am. Vet. Med. Assoc.*, **120**, 28-30 (1952).
- (5) Ehrlich, J., Bartz, Q. R., Smith, R. M., Joslyn, D. A., and Burkholder, P. R., *Science*, **106**, 417 (1947).
- (6) Ehrlich, J., Gottlieb, D., Burkholder, P. R., Anderson, L. E., and Pridham, T. G., *J. Bacteriol.*, **56**, 467-77 (1948).
- (6a) *Federal Register*, **14**, 5015-56 (1949); and numerous subsequent amendments, the latest (a recodification) in **19**, 1141 (1954).
- (7) Glazko, A. J., Edgerton, W. H., Dill, W. A., and Lenz, W. R., *Antibiotics & Chemotherapy*, **2**, 234-42 (1952).
- (8) Glazko, A. J., Wolf, L. M., and Dill, W. A., *Arch. Biochem.*, **23**, 411-18 (1949).
- (9) Glazko, A. J., Wolf, L. M., Dill, W. A., and Bratton, A. C., Jr., *J. Pharm. Exptl. Therap.*, **96**, 445-59 (1949).
- (10) Gottlieb, D., Bhattacharyya, P. K., Anderson, H. W., and Carter, H. E., *J. Bacteriol.*, **55**, 409-17 (1948).
- (11) Gottlieb, D., and Diamond, L., *Bull. Torrey Botan. Club*, **78**, 56-60 (1951).
- (12) Gruhzit, O. M., Fiske, R. A., Reutner, T. F., and Martino, E., *J. Clin. Invest.*, **28**, 943-52 (1949).
- (13) Hess, G. B., *Anal. Chem.*, **22**, 649-51 (1950).
- (13a) Higuchi, T., and Bias, C. D., *J. Am. Pharm. Assoc., Sci. Ed.*, **42**, 707-14 (1953).
- (13b) Higuchi, T., Marcus, A. D., and Bias, C. D., *J. Am. Pharm. Assoc., Sci. Ed.*, **43**, 135-39 (1954).
- (14) Holland, D. O., Jenkins, P. A., and Nayler, J. H. C., *J. Chem. Soc.*, **1953**, 273-80 (1953).
- (15) Joslyn, D. A., and Galbraith, M., *J. Bacteriol.*, **59**, 711-16 (1950).
- (15a) Lewis, C. N., Putnam, L. E., Hendricks, F. D., Kerlan, I., and Welch, H., *Antibiotics & Chemotherapy*, **2**, 601-08 (1952).
- (16) Ley, H. L., Jr., Smadel, J. E., and Crocker, T. T., *Proc. Soc. Exptl. Biol. Med.*, **68**, 9-12 (1948).
- (17) Long, L. M., and Troutman, H. D., *J. Am. Chem. Soc.*, **71**, 2469-72 (1949).
- (18) Long, L. M., and Troutman, H. D., *J. Am. Chem. Soc.*, **71**, 2473-75 (1949).
- (19) Matsuoka, M., Yagishita, K., and Umezawa, H., *Japan. J. Med. Sci. & Biol.*, **6**, 161-69 (1953).
- (20) McLean, I. W., Jr., Schwab, J. L., Hillegas, A. B., and Schlingman, A. S., *J. Clin. Invest.*, **28**, 953-63 (1949).
- (21) Mohrhoff, W. H., and Mogerman, W. D., *Proc. Indus. Quart.*, **12**, No. 1, 1-14 (1949).
- (22) Ogata, K., Shibata, M., Ueno, T., and Nakazawa, K., *J. Antibiotics (Japan)*, **4**, Suppl. A, 44-47 (1951).
- (23) Okami, Y., *Japan. Med. J.*, **1**, 499-503 (1948); *J. Antibiotics (Japan)*, **2**, 593-98 (1949).
- (24) Olive, T. R., *Chem. Eng.*, **56**, 107-13, 172-75 (1949).
- (25) Randall, W. A., Kirshbaum, A., Nielsen, J. K., and Wintermere, D., *J. Clin. Invest.*, **28**, 940-42 (1949).
- (26) Rebstock, M. C., Crooks, H. M., Jr., Controulis, J., and Bartz, Q. R., *J. Am. Chem. Soc.*, **71**, 2458-62 (1949).
- (26a) Saslaw, S., Stevenson, T. C., and Doan, C. A., *Proc. Soc. Exptl. Biol. Med.*, **85**, 295-97 (1954).
- (27) Schirmer, R. G., Eads, F. E., and Newman, J. P., *Vet. Med.*, **46**, 485-90 (1951).
- (28) Smadel, J. E., and Jackson, E. B., *Science*, **106**, 418-19 (1947).
- (29) Smith, D. G., Landers, C. B., Forgaes, J., *J. Lab. Clin. Med.*, **36**, 154-57 (1950).
- (30) Smith, R. M., Joslyn, D. A., Gruhzit, O. M., McLean, I. W., Jr., Penner, M. A., and Ehrlich, J., *J. Bacteriol.*, **55**, 425-48 (1948).
- (31) Umezawa, H., Kametani, R., Osato, T., Takeda, K., Kanari, H., Uehara, R., Kawahara, A., and Wada, R., *J. Antibiotics (Japan)*, **2**, 95-103 (1949).
- (32) Umezawa, H., and Maeda, K., *J. Antibiotics (Japan)*, **3**, 41-52 (1949).
- (33) Umezawa, H., Tazaki, T., Okami, Y., and Fukuyama, S., *Japan. Med. J.*, **2**, 207-11 (1949); *J. Antibiotics (Japan)*, **3**, 292-96 (1950).
- (34) Welch, H., and Lewis, C. N., *Antibiotic Therapy*, Arundel Press, Washington, D.C., 1951, ch. VII.
- (34a) Welch, H., Lewis, C. N., and Kerlan, I., *Antibiotics & Chemotherapy*, **4**, 607-23 (1954).
- (34b) Weston, J. K., Reutner, T. F., Thompson, R. Q., and Maxwell, R. E., *Federation Proceedings*, **13**, 416; *C.A.*, 1364 (1954).
- (35) Yagishita, K., and Umezawa, H., *Japan. Med. J.*, **3**, 289-97 (1950); *J. Antibiotics (Japan)*, **4**, 441-49 (1951).
- (36) U.S. Pat. 2,662,906 (Dec. 15, 1953), W. H. Edgerton (to Parke, Davis).

## NEOMYCIN

Neomycin, N.N.R., is a water-soluble basic antibiotic produced by *Streptomyces fradiae* and certain other species of *Streptomyces*. The original strain of *S. fradiae* isolated by Waksman and Lechevalier in 1948 was found to produce two isomeric substances, now recognized as neomycin B and neomycin C. Commercial neomycin is probably composed mainly of neomycin B and is usually in the form of a sulfate, a white amorphous powder. Neomycin mineral salts have not yet been crystallized. Neomycin is active against Gram-positive, Gram-negative, and acid-fast bacteria.

Clinically, neomycin is used topically in the treatment of bacterial infections of the skin and orally in the treatment of bacterial infections of the digestive tract. It can also be used systemically in the treatment of deep-seated bacterial infections that are resistant to other less toxic antibiotics.

The neomycin-producing culture of *S. fradiae* was isolated during a search at the laboratories of the Department of Microbiology, New Jersey Agricultural Experiment Station, Rutgers University, for antibiotics active against tubercle bacilli that had become resistant to streptomycin (9). The isolated neomycin was found to be very active against pathogenic mycobacteria, but when administered parenterally, it proved to be more toxic than streptomycin, especially upon the auditory canal. It has, however, certain desirable properties such as great stability, wide antibacterial spectrum, and water solubility, that make it a useful chemotherapeutic agent for the purposes mentioned. Neomycin is also nonirritant, nonallergenic, and relatively nontoxic when taken by mouth due to its lack of absorption from the digestive system. The development of microbial resistance to neomycin is also much slower than with streptomycin.

Other cultures producing neomycin or closely related substances were isolated by several Japanese workers, who called their preparations "flavomycin" and "streptothricin BI and BII." Peck *et al.* isolated from the neomycin complex a derivative of neomycin, which they called *neomycin A*. Its identity with *neamine*, a hydrolytic product of neomycin, was shown by Leach and Teeters (4). Regna and Murphy isolated *neomycin B* in 1950 (7), and Dutcher and coworkers (1), in 1951, showed that another substance, *neomycin C*, was also present in the culture filtrates of *S. fradiae*. Neomycin B and C proved to be isomers, and the empirical formula  $C_{29}H_{58}N_8O_{16}$  was assigned to them (1). The clinical value of neomycin was demonstrated by various workers (5,6,10). A review of the information available on neomycin was edited by Waksman (8).

## Physical and Chemical Properties

The inorganic acid salts of neomycin are highly water-soluble but are insoluble in organic solvents except methanol, in which limited solubility of the hydrochloride has been demonstrated. The optical rotation,  $[\alpha]_{25}^D$ , of neomycin B hydrochloride is  $+54^\circ$ , neomycin B sulfate  $+58^\circ$ , and neomycin C hydrochloride  $+80^\circ$  (all rotation measurements taken in water,  $c = 0.5\%$ ). Neomycin is a basic antibiotic, as shown by its ability to interact with acids to form salts and by its adsorption on cationic but not on anionic exchangers. The antibiotic is fairly stable over a pH range of 2.0–9.0. At these two extreme pH values, solutions of neomycin can be held at  $25^\circ\text{C}$ . for at least 1 day without loss of activity. Neomycin can be treated under a reflux condenser for 18 hours with an excess of barium hydroxide without loss of potency. It gives positive Molisch and carbazole tests for carbohydrate

residues; a negative Elson-Morgan test for glucosamine; a positive ninhydrin test; and shows no acidic or carbonyl groups. Neomycin does not reduce Fehling's or Tollens' reagents and it contains no methoxyl groups. Van Slyke determinations indicate that all the nitrogen is present in primary amino groups. Infrared studies suggest that polyamide linkages and some free amino groups are present in the molecule; and no absorption due to aromatic rings is found. Neomycin shows no absorption in the ultraviolet. Unlike streptomycin, neomycin does not yield maltol on alkaline hydrolysis. Acid hydrolysis, however, yields furfural and an organic base. Methanolysis of the hydrochlorides of neomycin B and C yields the following two fragments (1): (1) an amorphous hydrochloride, identical for both neomycin B and C, which is devoid of reducing power, yields all its nitrogen as amino nitrogen, and has the empirical formula  $C_9H_{19}N_3O_5 \cdot 3HCl$ ; and (2) nonidentical methyl glycosidic moieties, methyl neobiosaminiides B and C. The reducing diamines from the two methyl neobiosaminiides are not identical. The remainder of the molecules seems to be a pentose, as evidenced by the formation of furfural on acid hydrolysis.

### Preparation

Details of the commercial manufacture of neomycin have not been disclosed, but in the laboratory, neomycin can be produced by the following method:

A good neomycin-yielding strain of *S. fradiae* is grown in yeast extract medium (1% yeast extract, 1% commercial glucose in tap water, at pH 7.0) for 48 hours, at 28°C., on rotary shaking machines. A volume of 75 ml. of medium in 250-ml. Erlenmeyer flasks gives good results. Each of these flasks is used to inoculate one 2000-ml. Erlenmeyer flask containing 300 ml. of a casein hydrolyzate-beef extract medium (2.5% casein hydrolyzate (N-Z-amine), 1% beef extract (Bacto), tap water, pH 7.0); a chemically defined medium that may be used for neomycin production consists of L-proline, 15 grams; glucose, 10 grams; NaCl, 5 grams;  $K_2HPO_4$ , 2 grams;  $MgSO_4 \cdot 7H_2O$ , 1 gram;  $CaCl_2$ , 0.4 gram;  $FeSO_4 \cdot 7H_2O$ , 20 milligrams;  $ZnSO_4 \cdot 7H_2O$ , 10 milligrams; in one liter of distilled water, pH 7.0. The large flasks are incubated on rotary shaking machines at 28°C. for four days. The broth contains 500-1000  $\gamma$ /ml. of neomycin and has a pH of about 9.0. The mycelium is removed from the broth by filtration on paper. The pH of the filtrate is adjusted to 2.0 and the filtrate is agitated with 0.5% charcoal (Dareco G-60). The charcoal is filtered off, removing some impurities, and the pH adjusted to 7.0. The filtrate is then passed through a column of the weakly acidic cation exchanger (IRC50). In general, 1 ml. of sodium IRC50 is used for every 66 mg. of neomycin. The antibiotic held by the resin is eluted from the column with 0.1 N HCl. To remove the acid, the eluate is then passed through a column containing about 7.5 times as much of the anion exchanger IRA400 as of IRC50 used in the first column. The eluate is concentrated *in vacuo* to a small volume and neutralized with the appropriate acid; solid neomycin salt is obtained by lyophilization. This method furnished a yield of about 70% solids having a potency of 330 to 660  $\gamma$ /ml. (8).

Essentially pure neomycin can also be produced by adsorption on carbon and elution with aqueous acetone (3).

Neomycin is manufactured in the United States by the Heyden Division of American Cyanamid Co.; Upjohn Company; Commercial Solvents Corp.; E. R. Squibb and Sons; Chas. Pfizer and Co.; Merck and Co. Inc.; and S. B. Penick and Co.

As of January 1, 1954, the price of neomycin was \$0.60 per gram of pure base, and the production of neomycin was approximately 250 kg. a month.

Neomycin is available in a number of forms: (1) neomycin sulfate powder to make solutions for injections or for irrigation of fistulas and wounds; (2) neomycin ointments; (3) neomycin-bacitracin ointments; (4) neomycin-gramicidin ointments. (All three of these ointments are for treatment of skin or eye infections.) (5) Neomycin-cortisone ophthalmic ointment; (6) neomycin-bacitracin tablets; (7) neomycin-Kaopectate combination; and (8) neomycin-sulfa combination. The last three are for use in gastrointestinal infections.

A neomycin ointment (Teatube) is available for the treatment of bovine mastitis.

### Microbiological Properties

Neomycin is active *in vitro* against Gram-positive and Gram-negative bacteria. It is also active against mycobacteria and certain protozoa, but has no activity against anaerobic bacteria, fungi, rickettsiae, and viruses (8). Development of resistance to neomycin is a slower process as compared to streptomycin.

In experimental animals, neomycin shows activity against a variety of bacterial and mycobacterial diseases, including experimental tuberculosis.

### Pharmacological Properties

The LD<sub>50</sub> for subcutaneous injection of neomycin sulfate in mice is 125 mg./kg. and the LD<sub>50</sub> is 165-250 mg./kg. The LD<sub>50</sub> for intraperitoneal administration is about the same as that for subcutaneous injection. Intravenously, the neomycin preparations are about five times as toxic. Orally, the LD<sub>50</sub> is greater than 2800 mg./kg.

When given by injection, neomycin is well distributed in the body fluids. When given orally, it is but little absorbed through the intestinal wall. When given in high enough concentration for a long enough time, neomycin caused kidney damage and eighth cranial nerve disturbances leading to deafness. Applied topically or given orally, neomycin is markedly nontoxic, nonirritating, and has a low index of allergenicity.

### Specifications and Assay

Both biological and chemical methods are used for the evaluation of neomycin. The activity of neomycin against a given strain of *Escherichia coli* is taken as a standard. The activity of commercial preparations is expressed in micrograms of pure neomycin base/mg.

In the standardization of neomycin by the Food and Drug Administration, the cup method (see Vol. 2, p. 8) is used with *Staph. aureus* (*Micrococcus pyogenes* var. *aureus*) (A.T.C.C. 9144) as the test organism (2). The Food and Drug Administration specifications for neomycin are: (1) It should have a potency of no less than 330  $\gamma$ /ml.; (2) the product should be nontoxic to mice when injected intravenously at the rate of 100  $\gamma$ /20-gram mouse; (3) the product should contain no more than 8% moisture; (4) the pH of an aqueous solution containing 33 mg./ml. should be not less than 5 and not more than 7.5.

The use of ninhydrin (1,2,3-indantrione hydrate) has been proposed (8) as a rapid method of evaluation of neomycin by reaction of its amino group. An aqueous

solution of the antibiotic is heated with a solution of ninhydrin at a pH of 5.5–7.0; the color produced is blue-violet. The density of the solution is read at 570 m $\mu$ . The concentration of the neomycin is determined from the standard curve, and the result expressed in micrograms per milliliter. The reaction is not specific for neomycin, and hence, as a method of assay, it can only be applied to essentially purified samples, free from other compounds that give a color with ninhydrin.

### Uses

The chemotherapeutic role of neomycin is limited mainly to the treatment of bacterial infections of the skin, eyes, and oronasal cavity which can be treated topically and to the treatment of enteric bacterial infections. Neomycin is often used in combination with bacitracin or gramicidin. In ophthalmology, neomycin is also used in combination with cortisone.

For topical application advantages of neomycin are: great efficacy in suppressing the growth of many microorganisms, low index of allergic sensitization, low irritancy and local toxicity, low absorption from the skin or the wound, and great stability. However, if resistance should develop in organisms that might cause a systemic infection, there is an advantage in having used neomycin topically first because other antibiotics (such as the tetracyclines) which are less toxic systemically than neomycin can still be used subsequently if necessary.

Neomycin-sensitive strains do not readily develop resistance to the antibiotic.

As an intestinal antibiotic the advantages of neomycin are: wide antimicrobial spectrum, low toxicity due to limited absorption, chemical stability in the presence of the digestive enzymes and food, rapidity of action, limited development of bacterial resistance, and noninterference with tissue growth and repair. Neomycin is given orally to combat bacterial diarrheas. In this case neomycin can be combined with bacitracin or some bacterial adsorbent such as Kaopectate.

Neomycin has been used parenterally in the treatment of bacterial infections caused mainly by Gram-negative organisms. The results obtained were often very good, but the chronic toxicity of neomycin is such that its parenteral use should be limited to infections caused by organisms sensitive to neomycin and resistant to less toxic medication.

Neomycin has been used to treat a number of tuberculosis patients (8). The clinical response to neomycin was felt to be equivalent to that observed with *p*-aminosalicylic acid (PAS) or tibione but inferior to the already available therapeutic regimen of streptomycin and PAS used together. Use of neomycin in tuberculosis therapy was therefore discontinued.

The administration of neomycin can result, as in the case of many other antibiotics, in a stimulation of the fungal flora either of the skin or of the bowels.

For veterinary medicine, special neomycin ointments are available as for the treatment of bovine mastitis.

Neomycin does not seem to have any outstanding growth-promoting action in animals.

### Bibliography for Neomycin

- (1) Dutcher, G. D., Hosansky, N., Donin, M. N., and Wintersteiner, O., *J. Am. Chem. Soc.*, **73**, 1384 (1951).

- (2) Food and Drug Administration, *Federal Register*, **16**, 4964 (1951).
- (3) Leach, B. E., De Vries, W. H., Nelson, H. A., Jackson, W. G., and Evans, J. S., *J. Am. Chem. Soc.*, **73**, 2797-2800 (1951).
- (4) Leach, B. E., and Teeters, C. M., *J. Am. Chem. Soc.*, **74**, 3187 (1952).
- (5) Livingood, C. S., Nilasena, S., King, W. C., Stevenson, R. A., and Mullins, J. F., *J. Am. Med. Assoc.*, **148**, 334 (1952).
- (6) Poth, E. J., Fromm, S. M., Wise, R. I., and Hsiang, C. M., *Texas Repts. Biol. Med.*, **8**, 353 (1950).
- (7) Regna, P., and Murphy, F., *J. Am. Chem. Soc.*, **72**, 1045 (1950).
- (8) Waksman, S. A., *Neomycin*, Rutgers University Press, New Brunswick, N.J., 1953.
- (9) Waksman, S. A., and Lechevalier, H. A., *Science*, **109**, 305 (1949).
- (10) Wolgamot, J. R., and Duncan, G. G., *Penn. Med. J.*, **53**, 1264 (1950).

SELMAN A. WAKSMAN AND H. A. LEICHEVALIER

### ERYTHROMYCIN

Erythromycin N.N.R. (Ilotycin, Erythrocin) was described and made available as a chemotherapeutic agent in 1952. The antibiotic is produced by a strain of *Streptomyces erythreus*, isolated from a soil sample collected in the Philippines (56,81). Additional strains, not certainly identified as *S. erythreus*, which produce erythromycin have subsequently been isolated from soils originating in the United States and other parts of the world (51,56,81).

The antibiotic has a low degree of toxicity and is effective in the treatment of infections caused by some Gram-positive and Gram-negative bacteria, including strains resistant to penicillin (*q.v.*) and the "broad-spectrum" antibiotics.

Erythromycin is commercially available as the free base and as the stearate, glucoheptonate, and ethyl carbonate.

#### Physical and Chemical Properties

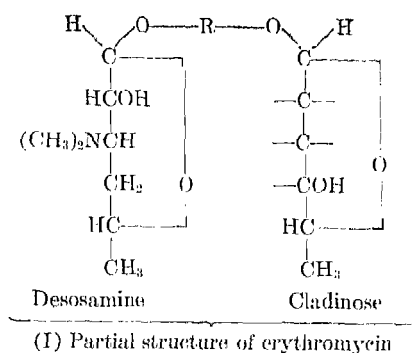
Erythromycin, (I) is a white, crystalline, basic compound, m.p. 134-38°C.,  $[\alpha]_D^{25} -78^\circ$  ( $c = 1.99\%$  in ethyl alcohol); it appears to have the empirical formula  $C_{37}H_{67-69}NO_{13}$ , based on analytical data and x-ray molecular weight values (19). Erythromycin exists as a dihydrate when crystallized from water (a number of other solvated forms exist governed by the solvent used for crystallization). The observed crystalline forms of erythromycin base exhibit water solubilities in the range 0.7-2.0 mg./ml. at 25°C. The antibiotic is highly soluble in alcohols, acetone, chloroform, acetonitrile, and ethyl acetate, and is moderately soluble in ether, ethylene dichloride, and amyl acetate (19,56,81).

The antibiotic has a single broad ultraviolet absorption band with a molar absorptivity of 26 at its maximum of 289 m $\mu$ . The infrared spectrum of a 5% solution of erythromycin in chloroform has been measured (19,56).

On the basis of available data, the partial structure (I) has been postulated for erythromycin. The  $pK'_a$  of erythromycin is 8.7 in both water and 66% dimethylformamide. It contains a dimethylamino group, one methoxyl group, and has a high C-methyl content (18%, 8 or more per mole) (19).

The degradation of erythromycin has been described (6,19,32). Mild acid hydrolysis yields *erythralosamine*, probably  $C_{29}H_{49}NO_8$ , and *cladinose*,  $C_8H_{16}O_4$ , a deoxy sugar containing one methoxyl group. Strong acid hydrolysis of erythromycin or erythralosamine yields *desosamine*,  $C_8H_{17}NO_3$ , a dimethylaminotrideoxyaldohexose

thought to have the structure shown in (I) (devoid of configuration), together with propionaldehyde.

(R = C<sub>21</sub>H<sub>36-38</sub>O<sub>6</sub>; the 5 bonds are to CH<sub>3</sub>, OCH<sub>3</sub>, 3H)

Alkaline hydrolysis of erythromycin yields a compound which contains a free carboxyl group and behaves like a zwitterion. This behavior is thought to indicate the presence of a lactone grouping in erythromycin as the zwitterion obtained has the same number of carbon atoms as erythromycin.

Acid addition salts of erythromycin are readily formed by treatment of aqueous erythromycin base with an equivalent of acid, or by the addition of acid to a solvent solution of erythromycin base. In the latter case, the salt may precipitate from the solvent in crystalline form. The salts formed with mineral acids are moderately unstable. Several salts of erythromycin have been prepared, among them the hydrochloride, sulfate, citrate, palmitate, stearate, and glucoheptonate (51,56,75,81).

Erythromycin reacts readily with acid chlorides to form esters, and the preparation of a number of such compounds has been described. By using the appropriate chlorocarbonate the ethyl carbonate, allyl carbonate, and benzyl carbonate esters of erythromycin have been prepared (57). Using acyl chlorides, normal esters such as the benzoate, caproate, caprylate, and palmitate have been made. Monoesters of dicarboxylic acids, such as erythromycin glutarate, succinate, maleate, and phthalate, result when erythromycin is reacted with cyclic anhydrides (74). A decrease in basicity of erythromycin is observed on acylation. It is believed that this indicates the esterified hydroxyl is on a carbon adjacent to the one bearing the dimethylamino group.

Erythromycin is oxidized by hydrogen peroxide, forming the *N*-oxide. Periodate also oxidizes the antibiotic to the *N*-oxide.

## Preparation and Manufacture

Erythromycin production by *Streptomyces erythreus* was initially demonstrated by the agar cross-streak technique. *S. erythreus* produces both erythromycin and a closely related product, *erythromycin B* (62), when cultivated at 28–32°C. in a suitable nutrient broth in shaken Erlenmeyer flasks. The antibiotic is found predominantly in the filtered culture broth. Representative nutrient media for each stage in the production of erythromycin are presented in Table I. When complex media containing crude substances of natural origin are used for production of vegetative inoculum (stage *B*), the mycelium should be washed before using it to inoculate the fermentation medium (stage *C*).

TABLE I. Nutrient Media for Erythromycin Fermentation.

<i>A</i> Sporulation agar (51)	<i>B</i> <i>Vegetative</i> inoculum medium (81)	<i>C</i> Fermentation medium (17)
20 g. starch	15 g. starch	25 g. starch
		25 g. glucose
1 g. asparagine	15 g. soybean meal	47 g. soybean meal
3 g. beef extract (Difco)	5 g. corn steep solids	10 g. corn steep solids
		5 g. yeast (brewer's)
20 g. agar	5 g. NaCl	5 g. NaCl
1000 ml. H <sub>2</sub> O	3 g. CaCO <sub>3</sub>	2 g. CaCO <sub>3</sub>
	1000 ml. H <sub>2</sub> O	Trace CoCl <sub>2</sub>
		1000 ml. H <sub>2</sub> O

Erythromycin can also be produced in laboratory equipment in a chemically defined medium such as the one following (62): 68.4 g. sucrose, 7.5 g. glycine, 0.9 g. DL-alanine, 5.0 g. K<sub>2</sub>HPO<sub>4</sub>, 5.0 g. NaCl, 0.5 g. MgSO<sub>4</sub>·7H<sub>2</sub>O, 0.02 g. FeSO<sub>4</sub>·7H<sub>2</sub>O, 0.01 g. ZnSO<sub>4</sub>·7H<sub>2</sub>O, 0.008 g. MnCl<sub>2</sub>·4H<sub>2</sub>O, 0.001 g. CoCl<sub>2</sub>·6H<sub>2</sub>O, 3.0 g. CaCO<sub>3</sub>, 1.0 liter H<sub>2</sub>O, pH (before sterilization) 7.5, pH (after sterilization) 7.1. This medium is suitable for both the vegetative inoculum and fermentation stages. If agar is added to form a solid substrate, this medium can also be used for sporulation, although media such as *A* in Table I are better for this purpose.

The starting pH of practical media (see Table I) is usually around pH 6.0, from which there is a small drop to 5.5–5.8, followed by a gradual rise to 7.2–7.5 or even 8.0 if the fermentation is allowed to continue. When the chemically defined medium is inoculated after sterilization the pH drops to 6.0 after four days and rises to 8–8.5 at the time of maximum potency (6 days).

Spores are produced in test tube cultures on medium *A* at 28–37°C. for 7–12 days. An aqueous spore suspension from a test tube culture is used to inoculate sterile medium *B* in Erlenmeyer flasks, which are incubated 2–4 days on a shaker at 28°C. The rapidly growing culture is then transferred to a similar medium previously sterilized in a fermentor, where it is incubated at 28°C. with continuous aeration and stirring. This fermentation may be harvested after 4–6 days in the fermentors (5–7 days if shaken flasks are used) or the rapidly growing culture may be used, after incubation for 1–3 days, to inoculate a large fermentor containing previously sterilized medium *C*. The inoculated medium is constantly stirred and aerated with sterile filtered air at 28°C. Foaming is controlled by the addition, as needed, of heat-sterilized antifoam substances, such as lard oil or commercial preparations.

Frequent samples, taken periodically throughout the fermentation, are checked for contamination, potency, pH, carbohydrate consumption, etc. When the rate of rise in potency begins to level off and the pH approaches 7.5–8.0, it is time to harvest.

Yields in shaken flasks and fermentors with capacities of 5–12,000 gallons, vary from a few hundred γ/ml. to 1 mg. or more per milliliter of broth (51,81). The final yield is influenced by controllable variables such as nutrients used, temperature, aeration rate, and stirring rate. Other variables which cannot be held entirely constant, such as the age of the stock culture used, exact growth stage of the inoculum, variability of crude nutrients, type and amounts of contamination which may gain entrance, and amount of antifoam introduced, may also have considerable influence upon the final yield.



**Extraction and Purification.** At the end of the fermentation period the whole culture broth is adjusted to pH 9.5 with sodium hydroxide and clarified by filtration with an inactive filter aid (Hyflo-Supercel). The clear broth is then extracted with an organic solvent, such as amyl acetate or ethyl acetate. Crude crystalline erythromycin can be obtained by concentration of the solvent extract, but greater purity is achieved by extraction back into water adjusted to pH 5.0 with sulfuric acid. The aqueous extract is then adjusted to pH 8.0 with sodium hydroxide, and concentrated *in vacuo* to a small volume. This concentrate is adjusted to pH 9.5 with aqueous sodium hydroxide, and is allowed to stand until crystallization occurs. The crystals are recovered by filtration. The mother liquor is adjusted to pH 8.0 with dilute sulfuric acid and concentrated considerably *in vacuo*. The solution is adjusted to pH 9.5 again and allowed to stand, whereupon a second crop of crystals is formed. Several recrystallizations from warm aqueous acetone result in a highly purified crystalline base preparation (6,51,81).

Extraction of culture broths at an alkalinity lower than pH 9.0 may result in a product quite different from the base. This has been partially described as an erythromycin complex (81).

Crude aqueous erythromycin can also be purified by adsorption on a magnesium aluminum silicate column, washing the silicate with 5% methanol in benzene, and eluting with 50% methanol in benzene. The eluate is then evaporated to dryness. Final purification is obtained by repeated recrystallization from aqueous acetone.

Erythromycin is manufactured in the United States by Eli Lilly and Company, Abbot Laboratories, and the Upjohn Company.

**Market Forms.** Erythromycin is marketed as the crystalline base in the form of coated, acid-resistant tablets both alone and in combination with sulfonamides. The base is also packaged in ointment form, alone and in combination with neomycin. As erythromycin ethyl carbonate, the antibiotic is available, alone and in combination with sulfonamides, to be suspended in water for oral pediatric use. Erythromycin stearate is also marketed in tablet form and as a suspension for oral pediatric use. The glucoheptonate is available for intravenous administration.

**Stability.** Erythromycin base is completely stable for at least 1½ years when stored at 50°C., but loses 25–30% of its activity after 1 month at 100°C. Aqueous solutions and suspensions of erythromycin at room temperature are most stable in the pH range 6–8, deteriorating rapidly below pH 5.0 and slowly at pH 8.5 or above (81). Solutions in physiologic saline retain full activity for about three days at room temperature (35) and in broth for four days at 37°C. (29). Solutions are stable at 60°C. for 5 minutes but show a slight loss after 15 minutes (29).

The ethyl carbonate ester of erythromycin retains full strength for at least 6 months at 50°C.; in aqueous suspension, it very slowly deteriorates at the same temperature, losing 10–15% of its activity in 3–6 months.

### Microbiological Properties

**Range of Activity.** The antimicrobial spectrum originally described for erythromycin (56,81) has been verified and extended by numerous investigators (18,22,23,25,29,30,35,42,55,64,67,71,78). In general, erythromycin has a penicillin-like antibacterial spectrum, but it also affects several types of organisms that are not sensitive to penicillin. It is most strikingly active against the pathogenic cocci, including

nearly all strains of staphylococci and streptococci freshly isolated from patients (13,16,22,29,35,39,52,77,79). Many of the pathogenic Gram-positive bacilli, certain Gram-negative species such as *Neisseria*, *Hemophilus*, *Brucella*, and *Pasteurella*, and at least one species of *Actinomyces* are highly sensitive. The antibiotic is, like penicillin, strongly active against spirochetes such as *Borrelia novyi* (55), *Treponema pallidum* (42), and *Leptospira icterohemorrhagiae* (60). It shows significant activity also against *Endamoeba histolytica*, trypanosomes, oxyurids (55), and rickettsiae (35,56,64). Mycobacteria are only moderately sensitive. Bacteria of the colon-typhoid group, enterococci in general, fungi and pleuropneumoniae-like organisms (42) are for all practical purposes nonsensitive to erythromycin.

The antibacterial activity of erythromycin increases 5- to 10-fold with each pH unit increment in the pH range 5.5-9 (29,30,35,38,63). Activity is not significantly influenced by serum, glucose, or any of a large number of inorganic ions, metabolic intermediates, and organic substances which have been found to inhibit action of other antibiotics (29,30,56,63). Production of erythromycin-inactivating enzymes by microorganisms has not been observed (29,30,39).

Erythromycin is bactericidal at low concentrations for multiplying pneumococci, hemolytic streptococci, staphylococci, and corynebacteria, but has little killing effect upon mature or refrigerated cultures (29,30,35,64,67). Inoculum size influences the time required for total killing but not the actual rate of killing (29). Concentrations required for inhibiting several bacterial species are not greatly influenced by large increments in test inocula (25,29,30,63). Bacterial species which are highly sensitive with respect to inhibition vary greatly in their susceptibility to the bactericidal action of erythromycin, with respect to both rate and concentrations required for killing (35,64).

Erythromycin is highly effective by both oral and parenteral routes in protecting animals infected with pneumococci, diphtheria, hemolytic streptococci, *Hemophilus pertussis* (35,64,65), and *Borrelia novyi* (55,56). It has protective action in mice against rickettsial infections such as psittacosis, lymphogranuloma venereum, and mouse meningopneumonitis, and against epidemic typhus in embryonated eggs (35,55,56,64). *Trichomonas vaginalis*, *Toxoplasma*, *Trypanosoma equiperdum*, and oxyurid infections in mice, and *Endamoeba histolytica* infections in rats are suppressed or eliminated by erythromycin administered orally or parenterally (55,56). Slight protection is shown in mice against *Mycobacterium tuberculosis* (56). True viruses, including Lansing poliomyelitis and influenza A virus, are unaffected by erythromycin in animal tests (64).

Erythromycin is reported to be synergistic with streptomycin and with bacitracin (66,67). It is not synergistic with penicillin, oxytetracycline, or chloramphenicol (7,35,67). In animal chemotherapy studies, erythromycin has been found to act synergistically with sulfadiazine and at least additively with penicillin, bacitracin, and streptomycin (40,65).

**Development of Resistance.** Bacteria develop resistance to erythromycin *in vitro* in stepwise fashion, at a rate much more similar to that against penicillin than to the very rapid rate usually associated with streptomycin (22,29,30,35,39,56,63,66). Strains of *Micrococcus pyogenes* vary greatly in the rates at which they acquire resistance (22,35). Enterococci become resistant rapidly, pneumococci at a moderate rate, and strains of *Streptococcus pyogenes* and *S. viridans* very slowly (29). Cross resistance between erythromycin and other antibiotics has not been observed (12,14,22,35,

59,64,66,79) with the one exception, carbomycin, with which almost complete reciprocal cross resistance has been reported (7,17,18,22,39). Certain combinations of antibiotics, such as erythromycin-streptomycin and erythromycin-penicillin, may delay or prevent development of resistance by staphylococci and enterococci to either drug *in vitro* (17,29,66).

Resistance of staphylococci and streptococci to erythromycin occurs clinically chiefly in chronic or inaccessible infections (12,14,29,35,44,59,73), such as subacute bacterial endocarditis and osteomyelitis. Large-scale use of this antibiotic in hospitals results, just as with penicillin and the other major commercial antibiotics, in a rapid increase in the incidence of resistant staphylococci in patients and hospital personnel (50). How or why this occurs is not at present fully understood.

### Pharmacological Properties

**Absorption and Excretion.** Erythromycin is absorbed from the intestinal tract into the blood stream (2,35,56), from which it passes into the spinal fluid, amniotic fluid, saliva, bile, pancreatic juice, milk, and fetal serum of animals (36). High tissue concentrations are detectable after oral administration in all the visceral organs, the heart and other muscles, skin, reproductive organs, and various glands of the animal body. The highest concentrations are found in the liver and bile. All tissues except the brain contain higher concentrations than the serum and retain measurable concentrations longer than activity can be detected in the serum (48). Much greater absorption of erythromycin is obtained by oral administration of coated acid-resistant tablets than with plain gelatin capsules (2). On intravenous administration of erythromycin glucoheptonate in dogs, 33% of the total dose has been recovered in the bile and 16% in the urine (47). Some of the antibiotic found in the bile of dogs after intravenous injection of erythromycin glucoheptonate has been identified as a distinct, antibacterial metabolite of erythromycin (49).

In human subjects, oral administration of erythromycin in gelatin capsules in doses of 0.3 g. or more results in therapeutically effective serum concentrations over a period of six hours (29,35,73). Use of acid-resistant tablets results in higher, more predictable serum levels at an equivalent dosage (41,45,73). As in animals, the drug reaches the ascitic, pleural, and spinal fluids. Concentrations in spinal fluid of patients with noninflamed meninges are very low. The drug reaches high concentrations in the bile, feces, and urine (27,35). Erythromycin ethyl carbonate and erythromycin stearate, being highly insoluble, are markedly resistant to the destructive effect of the acidity of gastric secretions. Oral administration of these forms of erythromycin in suspension, therefore, results in effective blood concentrations (51,75). Serum concentrations of 0.5–10  $\gamma$ /ml. can also be maintained by the intravenous injection of erythromycin glucoheptonate, either by its rapid administration in high concentration or by continuous drip with dilute solutions (27,53).

**Toxicity.** The single-dose  $LD_{50}$  of erythromycin hydrochloride for mice by the intravenous route is 426 mg./kg. body weight. The oral  $LD_{50}$  of the hydrochloride or the base in mice is about 3.0 g./kg. Tests in the rat, hamster, rabbit, and dog confirm the low order of toxicity. Daily oral administration for three months of 100 mg. erythromycin (in plain gelatin capsules) per kilogram of body weight to dogs produces no damage to visceral organs, bone marrow, kidney function, or the formed elements of the blood. No eighth nerve damage was detectable in cats that received 50

mg./kg. daily for 10 weeks by the intramuscular route (2). Subcutaneous and intraperitoneal administration of 5 mg./ml. erythromycin base in aqueous solution in mice causes irritation at the site of injection (35,51).

In human adult subjects, repeated oral doses of 0.75-1.0 g. of erythromycin often cause gastrointestinal irritation, including nausea, vomiting, and occasionally diarrhea (35); no other systemic reaction was noted. With doses of 0.5 gram, side effects are infrequent and less severe, and smaller doses rarely cause significant disturbance (4,29,35,41,73). Study of several patients treated orally with erythromycin revealed no abnormalities in blood cell counts, plasma proteins, serum bilirubin, blood urea nitrogen, prothrombin time, cephalin flocculation, thymol turbidity, vestibular function, or audiograms (73). Erythromycin glucoheptonate is well tolerated by the intravenous route (27,53,72).

As a topical agent in ointment form, erythromycin appears to be relatively free of side effects such as skin irritation or sensitization (52,69,70).

*There have been no reports of anaphylactic reactions with erythromycin. One drug fever reaction has been reported (4).*

### Specifications and Assay

From the time of its introduction, erythromycin in all its marketed forms has been a pure, crystalline compound. There are no formal specifications of quality other than that each lot of the antibiotic must meet the standards of identity, purity, and safety set up by the manufacturer. These standards have been reviewed and approved by the Food and Drug Administration. Chemical and physical controls include tests for solubility, heavy-metal content, melting point, crystallinity, infrared absorption, and potentiometric titration. Each lot is tested for toxicity in mice by several routes, and microbiological potency assays are run on both the bulk material used in formulation and the final product.

The sensitivity of microorganisms to erythromycin is commonly measured in terms of minimum inhibiting concentrations on exposure of test organisms to serial dilutions of crystalline erythromycin base in nutrient broth or nutrient agar. The potency or purity of a preparation can be assayed microbiologically by agar diffusion -- inhibition zone techniques (see Vol. 2, p. 8) in which either assay cylinders or filter paper disks are used as receptacles for sample solutions, or by a broth turbidimetric procedure (38). Variations of these techniques have been adapted to the assay of erythromycin in serum and other body fluids (34,35,41,45,46,80).

Several chemical assays for erythromycin have been developed. One is based on a blue color reaction of the hydrolyzed antibiotic with an arsenomolybdate reagent, the optical density of the pigment being a function of concentration (61). Another depends upon a linear relationship between erythromycin concentration and infrared absorption (76). A third assay entails measurement of the intensity of a yellow color resulting from treatment of erythromycin solutions with strong sulfuric acid (20).

### Uses

Erythromycin has found its greatest usefulness in the treatment, by the oral route, of staphylococcal, streptococcal, and pneumococcal infections (10,21,26,29,35,37,44,56,69,72,73). Direct comparison of erythromycin with penicillin in a large series of streptococcal infections, scarlet fever (28), and pneumococcal infections (4)

indicated that the drugs are very similar in their efficacy. Fewer side effects were seen in the erythromycin-treated patients, however. Most notable is its general effectiveness against staphylococcal strains found resistant to penicillin and the broad-spectrum antibiotics (12,14,15,22,35,37,54,79). Results in the treatment of gonorrhea are generally favorable, but not comparable to those with penicillin (8,11,23,29). Other types of infections for which favorable results with erythromycin have been reported are pneumonia with bacteremia due to *Hemophilus influenzae* (58), diphtheria in carriers (29), meningococcemia (1), Donovanosis and syphilis (8), lymphogranuloma venereum (5,8), granuloma inguinale (68), amebic dysentery (3), brucellosis (31), and fusospirochetal infections of the mouth and throat (9). Some effect on the course of A' influenza virus infections has been described (10). Erythromycin glucoheptonate has proved useful for intravenous therapy in seriously ill patients (33,53,72). Very favorable therapeutic efficacy has been shown for erythromycin ointments in the treatment of pyogenic skin infections, the only undesirable effect being infrequent incidence of mild irritation or sensitization (21,52,69,70).

As with other drugs, erythromycin has not proved entirely reliable in subacute bacterial endocarditis, though it is sometimes effective (29,35,37,73). There is clinical evidence that erythromycin therapy in combination with streptomycin or bacitracin may form an effective regimen in endocarditis and severe staphylococcal infections (24,40,79). *Pseudomonas* and *Proteus* wound infections have failed to respond to erythromycin treatment (73). There is no indication for treatment of infections from Gram-negative bacteria of the colon-typhoid group or of fungus infections with this antibiotic.

### Bibliography

- (1) Anderson, E. A., *Antibiotics and Chemotherapy*, **3**, 1091-94 (1953).
- (2) Anderson, R. C., Harris, P. N., and Chen, K. K., *J. Am. Pharm. Assoc., Sci. Ed.*, **41**, 555-58 (1952).
- (3) Anderson, H. H., Nelson, T. L., Irenhoff, A. K., and Fish, C. H., *Am. J. Trop. Med. Hyg.*, **3**, 254-61 (1954).
- (4) Austrian, R., Rosenblum, R., Metz, M., Fox, L., Gelb, I. J., Rosenberg, B. A., and Kushner, D. B., *Am. J. Med. Sci.*, **226**, 487-90 (1953).
- (5) Banov, L., Jr., and Goldberg, J., *Antibiotics Annual*, **1953-1954**, 475-79.
- (6) Clark, R. K., Jr., *Antibiotics and Chemotherapy*, **3**, 663-71 (1953).
- (7) Coleman, V. R., Gunnison, J. B., and Jawetz, E., *Proc. Soc. Exptl. Biol. Med.*, **83**, 668-70 (1953).
- (8) Cordice, J. W. V., Jr., Avecilla, M., Marmell, M., Shidlovsky, B. A., and Prigot, A., *Antibiotics Annual*, **1953-54**, 480-84.
- (9) Cronk, G. A., and Naumann, D. E., *J. Lancet*, **2**, 462-63 (1953).
- (10) Cronk, G. A., and Naumann, D. E., *N.Y. State J. Med.*, **54**, 373-75 (1954).
- (11) David, N. A., Wellborn, W. S., and Smith, D. T., *Federation Proc.*, **12**, Pt. I, 314 (1953).
- (12) Dearing, W. H., and Heilman, F. R., *Proc. Staff Meetings Mayo Clinic*, **28**, 121-34 (1953).
- (13) Eisenberg, G. M., Flippin, H. F., and O'Loughlin, J. M., *Antibiotics and Chemotherapy*, **3**, 1026-28 (1953).
- (14) Dearing, W. H., Heilman, F. R., and Sauer, W. G., *Gastroenterology*, **26**, 38-47 (1954).
- (15) Finland, M., *Antibiotics Annual*, **1953-54**, 10-26.
- (16) Finland, M., and Haight, T. H., *Arch. Internal Med.*, **91**, 143-58 (1953).
- (17) Finland, M., and Wilcox, C., *Proc. Soc. Exptl. Biol. Med.*, **83**, 605-8 (1953).
- (18) Finland, M., Wilcox, C., Wright, S. S., and Purcell, E. M., *Proc. Soc. Exptl. Biol. Med.*, **81**, 725-29 (1952).
- (19) Flynn, E. H., Sigal, M. V., Jr., Wiley, P. F., and Gerzon, K., *J. Am. Chem. Soc.*, **76**, 3121-31 (1954).
- (20) Ford, J. H., Prescott, G. C., Hinman, J. W., and Caron, E. L., *Anal. Chem.*, **25**, 1195-97 (1953).

- (21) Freeman, L. C., and Scott, R. B., *J. Pediat.*, **42**, 669-72 (1953).
- (22) Fusillo, M. H., Noyes, H. E., Pulaski, E. J., and Tom, J. Y. S., *Antibiotics and Chemotherapy*, **3**, 581-86 (1953).
- (23) Gable, C. R., Romansky, M. J., and Taggart, S. R., *Am. J. Syphilis, Gonorrhea, Venereal Diseases*, **37**, 377-78 (1953).
- (24) Geraci, J. E., and Martin, W. J., *Proc. Staff Meeting Mayo Clinic*, **29**, 109-118 (1954).
- (25) Gorzynski, E. A., and Neter, E., *Antibiotics and Chemotherapy*, **3**, 1211-14 (1953).
- (26) Grigsby, M. E., Johnson, J. B., and Simmons, G. W., *Antibiotics and Chemotherapy*, **3**, 1029-34 (1953).
- (27) Griffith, R. S., Johnstone, D. M., and Smith, J. W., *Antibiotics Annual*, **1953-54**, 496-99.
- (28) Haight, T. H., *J. Lab. Clin. Med.*, **42**, 811 (1953); **43**, 15 (1954).
- (29) Haight, T. H., and Finland, M., *New England J. Med.*, **247**, 1-6 (1952).
- (30) Haight, T. H., and Finland, M., *Proc. Soc. Exptl. Biol. Med.*, **81**, 175-93 (1952).
- (31) Harris, H. J., *Antibiotics and Chemotherapy*, **3**, 982-89 (1953).
- (32) Hasbrouck, R. B., and Garven, F. C., *Antibiotics and Chemotherapy*, **3**, 1040-52 (1953).
- (33) Haviland, J. W., *Ann. Internal Med.*, **39**, 307-17 (1953).
- (34) Heilman, D. H., and Herrell, W. E., *Am. J. Clin. Path.*, **15**, 7-9 (1945).
- (35) Heilman, F. R., Herrell, W. E., Wellman, W. E., and Geraci, J. E., *Proc. Staff Meetings Mayo Clinic*, **27**, 285-304 (1952).
- (36) Henderson, F. G., Powell, C. E., Rose, C. L., and Robbins, E. B., *J. Pharmacol. Exptl. Therap.*, **106**, 395 (1952).
- (37) Herrell, W. E., Nichols, D. R., and Martin, W. J., *J. Am. Med. Assoc.*, **152**, 1601-6 (1953).
- (38) Higgins, C. E., Pittenger, R. C., and McGuire, J. M., *Antibiotics and Chemotherapy*, **3**, 50-54 (1953).
- (39) Hobson, D., *Brit. Med. J.*, **1954**, **1**, 236-38.
- (40) Jones, L. C., and Yow, E. M., *Antibiotics Annual*, **1953-54**, 464-69.
- (41) Josselyn, L. E., and Sylvester, J. C., *Antibiotics and Chemotherapy*, **3**, 63-66 (1953).
- (42) Keller, R., and Morton, H. E., *Am. J. Syphilis, Gonorrhea, Venereal Diseases*, **37**, 379-82 (1953).
- (43) Kirby, W. M. M., and Ahern, J. J., *Antibiotics and Chemotherapy*, **3**, 831-35 (1953).
- (44) Kirby, W. M. M., Forland, T., and Maple, F. M., *Arch. Internal Med.*, **92**, 464-70 (1953).
- (45) Kirby, W. M. M., Maple, F. M., and O'Leary, B., *Antibiotics and Chemotherapy*, **3**, 473-77 (1953).
- (46) Kirshbaum, A., Bowman, F. W., Wintermere, D. M., and Friedman, E. R., *Antibiotics and Chemotherapy*, **3**, 537-39 (1953).
- (47) Lee, C. C., Anderson, R. C., and Chen, K. K., *Antibiotics Annual*, **1953-54**, 485-92.
- (48) Lee, C. C., Anderson, R. C., and Chen, K. K., *Antibiotics and Chemotherapy*, **3**, 920-24 (1953).
- (49) Lee, C. C., Anderson, R. C., Bird, H. L., and Chen, K. K., *Antibiotics Annual*, **1953-54**, 493-95.
- (50) Lepper, M. H., Moulton, B., Dowling, H. F., Jackson, G. G., and Kofman, S., *Antibiotics Annual*, **1953-54**, 308-13.
- (51) Lilly Research Laboratories, unpublished data.
- (52) Livingood, C. S., Head, E. S., Johnson, E. A., and Nilasem, S., *J. Am. Med. Assoc.*, **153**, 1266-70 (1953).
- (53) Maple, F. M., O'Leary, B., and Kirby, W. M. M., *Antibiotics and Chemotherapy*, **3**, 836-39 (1953).
- (54) Martin, W. J., Nichols, D. R., and Geraci, J. E., *Proc. Staff Meetings Mayo Clinic*, **28**, 609-16 (1953).
- (55) McCowen, M. C., Callender, M. E., Lawlis, J. F., Jr., and Brandt, M. C., *Am. J. Trop. Med. and Hyg.*, **2**, 212-18 (1953).
- (56) McGuire, J. M., Bunch, R. L., Anderson, R. C., Boaz, H. E., Flynn, E. H., Powell, H. M., and Smith, J. W., *Antibiotics and Chemotherapy*, **2**, 281-83 (1952).
- (57) Murphy, H. W., *Antibiotics Annual*, **1953-54**, 500-13.
- (58) Nasou, J. P., Romansky, M. J., and Barr, J. F., *Antibiotics Annual*, **1953-54**, 470-74.
- (59) Needham, G. M., and Nichols, D. R., *J. Lab. Clin. Med.*, **41**, 150-56 (1953).
- (60) Ormsby, R. A., *Proc. Soc. Exptl. Biol. Med.*, **83**, 815-16 (1953).
- (61) Perlman, D., *Science*, **118**, 628-29 (1953).
- (62) Pettinga, C. W., Stark, W. M., and Van Abeele, F. R., *J. Am. Chem. Soc.*, **76**, 569-71 (1954).
- (63) Pittenger, R. C., Wolfe, R. N., and Marks, P. N., *Antibiotics Annual*, **1953-54**, 449-59.

- (64) Powell, H. M., Boniece, W. S., Pittenger, R. C., Stone, R. L., and Culbertson, C. G., *Antibiotics and Chemotherapy*, **3**, 165-82 (1953).
- (65) Powell, H. M., Culbertson, C. G., Boniece, W. S., Streightoff, F., Baker, L. A., and Metcalf, H. B., *Antibiotics and Chemotherapy*, **3**, 701-8 (1953).
- (66) Purcell, E. M., Wright, S. S., and Finland, M., *Proc. Soc. Exptl. Biol. Med.*, **82**, 124-31 (1953).
- (67) Rantz, L. A., and Randall, E., *Antibiotics and Chemotherapy*, **2**, 645-52 (1952).
- (68) Robinson, H. M., and Cohen, M., *J. Invest. Dermatol.*, **20**, 407-9 (1953).
- (69) Robinson, H. M., and Zeligman, I., *J. Invest. Dermatol.*, **20**, 405-6 (1953).
- (70) Schonberg, I. L., *Ohio State Med. J.*, **49**, 1099 (1953).
- (71) Shidlovsky, B. A., Marmell, M., Prigot, A., and Wright, L. T., *Antibiotics Annual*, **1953-54**, 548-59.
- (72) Shoemaker, E. H., and Yow, E. M., *Antibiotics Annual*, **1953-54**, 460-63.
- (73) Smith, J. W., Dyke, R. W., and Griffith, R. S., *J. Am. Med. Assoc.*, **151**, 805-10 (1953).
- (74) Stephens, V. C., *Antibiotics Annual*, **1953-54**, 514-21.
- (75) Sylvester, J. C., and Josselyn, L. E., *Antibiotics and Chemotherapy*, **3**, 930-32 (1953).
- (76) Washburn, W. H., *J. Am. Pharm. Assoc., Sci. Ed.*, **43**, 48-49 (1954).
- (77) Weil, A. J., and Stempel, B., *Antibiotics and Chemotherapy*, **3**, 1135-40 (1953).
- (78) Welch, H., Randall, W. A., Reedy, R. J., and Kramer, J., *Antibiotics and Chemotherapy*, **2**, 693-96 (1952).
- (79) Wise, R. I., and Spink, W. W., *Antibiotics Annual*, **1953-54**, 322-27.
- (80) Ziegler, D. W., and McGuire, J. M., *Antibiotics and Chemotherapy*, **3**, 67-70 (1953).
- (81) U.S. Pat. 2,653,899 (Sept. 29, 1953), R. L. Bunch and J. M. McGuire.

J. M. MCGUIRE AND E. H. FLYNN

## CARBOMYCIN

Carbomycin, N.N.R. (Magnamycin) is a product of the action of several actinomycetes identified as strains of *Streptomyces halstedii* (22) growing upon various culture media under aerobic conditions. A number of different soil samples have provided the microorganisms with which the antibiotic was produced. The organisms grow luxuriantly under submerged conditions. In addition, one strain produces a closely related antibiotic designated carbomycin B. Carbomycin is principally active against Gram-positive bacteria and a few Gram-negative types.

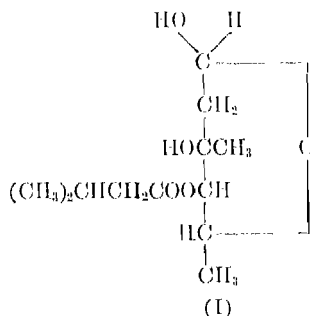
A review (12) of the chemistry and biological action of carbomycin was published in 1953.

### Physical and Chemical Properties

Carbomycin is a crystalline monobasic substance tentatively assigned the empirical formula  $C_{41-42}H_{67-69}NO_{16}$  (23). It crystallizes from methanol as colorless laths, m.p. 212-214°C. (decomp.),  $[\alpha]_D^{25} - 58.6$  ( $c = 1\%$  in chloroform). It is readily soluble in most polar organic solvents but is virtually insoluble in hydrocarbons and water. Carbomycin shows a neutral equivalent of 836 and  $pK_b$  7.2. It forms stable salts with mineral acids; the hydrochloride is readily soluble in water in contrast to the periodate salt which is quite insoluble. The antibiotic gives negative ninhydrin and Van Slyke nitrogen tests. It gives positive Fehling and Tollens tests. The presence of carbonyl groupings is suggested by a positive phenylhydrazine test. The antibiotic readily decolorizes permanganate and bromine. In the presence of strong mineral acids, it develops a characteristic deep violet color which slowly fades to red brown.

The ultraviolet absorption spectrum of carbomycin in 90% ethyl alcohol solution

shows a strong absorption peak  $\lambda$  238  $m\mu$  ( $E_{1\%}^{1\text{cm}}$  185) together with a much weaker peak at  $\lambda$  327  $m\mu$  ( $E_{1\%}^{1\text{cm}}$  0.9). The position and intensity of this pair of peaks are characteristic of  $\alpha,\beta$ -unsaturated ketones, and this assignment is consistent with the presence of absorption peaks at 5.95 and 6.15  $\mu$  in the infrared spectrum. Alkaline hydrolysis of carbomycin yields one mole each of acetic and isovaleric acids and dimethylamine. Controlled mild acid hydrolysis results in hydrolytic cleavage of the carbomycin into two fragments. The first product, *isovaleroylmucarose*, a viscous oil with the empirical formula  $C_{13}H_{22}O_5$ , has been shown to have the structure (I)



devoid of configurational implication (18). The second fragment, a crystalline solid, is a weak base which appears to have the molecular formula  $C_{29-30}H_{47-49}NO_{12}$ . Mild acid hydrolysis of this substance yields a crystalline dimethylamino sugar whose empirical formula is  $C_8H_{17}NO_4 \cdot HCl \cdot H_2O$ . Several biologically active derivatives of carbomycin have been prepared. For example, a diacetyl derivative, an oxime, and a thiosemicarbazone have been prepared by standard procedures. Hydrogenation over palladium-charcoal catalyst in ethyl alcohol results in prompt absorption of two moles of hydrogen and yields a crystalline tetrahydro derivative, which also forms a diacetate.

**Carbomycin B** (15) has the probable molecular formula  $C_{41-42}H_{67-69}NO_{15-16}$ , crystallizes as anisotropic plates, m.p.  $140^\circ\text{C}$ .,  $pK_b$  7.5, and has an equivalent weight of about 890. Carbomycin B appears to be much more soluble in organic solvents than carbomycin. It shows a marked similarity to carbomycin in most of its chemical and biological characteristics. The stability of carbomycin B parallels that of carbomycin. It forms a hydrochloride, thiosemicarbazone, monoacetyl derivative, and, on catalytic hydrogenation, a tetrahydro derivative which forms a monoacetate. On hydrolysis carbomycin B yields isovaleroylmucarose (I) and a second fragment which contains the same dimethylamino sugar moiety found in carbomycin. In contrast to carbomycin, carbomycin B contains an  $\alpha\text{-}\beta\text{-}\gamma\text{-}\delta$ -unsaturated carbonyl system. In absolute ethyl alcohol, it has an ultraviolet absorption peak at 278  $m\mu$  ( $E_{1\%}^{1\text{cm}}$  276) and a minimum of 230  $m\mu$  ( $E_{1\%}^{1\text{cm}}$  35). The infrared spectrum is virtually identical to that of carbomycin except in the 5.8–6.3 and the 10.3  $\mu$  regions.

### Preparation and Manufacture

The organism used for the production of carbomycin is a strain of *S. halstedii* but not all strains of this species are active. Those that are active may gain or lose ability to produce the antibiotic depending on the conditions under which they are maintained, age, etc.

Nutrient agar containing a small amount of yeast extract supplies a satisfactory culture medium. A temperature of  $27\text{--}28^\circ\text{C}$ . for seven days is suitable for incubation.



Spores obtained from such a culture are inoculated into liquid medium containing a source of carbohydrate, such as dextrose or starch; a source of nitrogen, such as casein, casein digest, or soybean meal; growth-stimulating substances, such as distiller's solubles or molasses fermentation residues; 0.5% sodium chloride; and sufficient calcium carbonate to maintain the medium at pH 6.5–7 during the two days required for growth of the submerged inoculum. A medium of the same type is used for the fermentation to which is added 5% of the above as inoculum. The same temperature and pH conditions employed in the preparation of the inoculum can be used. Depending on the size and type of equipment, a sterilization temperature of 120°C. should be maintained from 10 to 60 minutes. In general, the same type of equipment that is used for penicillin fermentation (see Vol. 9, p. 926) (1,2) with respect to agitation and aeration should prove successful for the carbomycin fermentation. The course of the fermentation is followed periodically by pH determination, weight of mycelium, and potency as determined by bioassay using a plate assay with *Bacillus subtilis* as the test organism (8).

When the potency reaches a maximum, generally in 2–3 days, the mycelium is separated from the fermentation broth on filter presses and the antibiotic is isolated from the filtered broth by conventional procedures, such as extraction with a water-immiscible solvent, for example, methyl ethyl ketone, at a pH close to neutrality, preferably in a continuous extractor. The solvent phase is concentrated to approximately 1/10 of its volume *in vacuo* and the antibiotic is extracted with water at about pH 2.0. The purification proceeds by alternate extraction with solvent at neutrality, then with water at pH 2.0, and finally with solvent at neutrality. Upon removing the solvent by distillation, the antibiotic crystallizes as white needles. The crude product can be recrystallized from alcohol–water mixtures, and very highly purified carbomycin can be obtained by repeated crystallizations from methanol.

By these processes, it is possible to produce carbomycin so that its price is competitive with that of "broad-spectrum" antibiotics.

### Microbiological Properties

Carbomycin is principally active against Gram-positive bacteria and a few Gram-negative microorganisms, such as *Neisseria catarrhalis* and *Hemophilus influenzae*, but has little effect on fungi (5). The activity of carbomycin is not altered appreciably in the presence of 1–20% concentration of human serum or when tested in four different laboratory media. The antibiotic is primarily a bacteriostatic agent although at certain concentrations, depending on the number of microorganisms present, it acts in a bactericidal manner. It acts only on multiplying bacteria. In general, about five times as much carbomycin is required to produce a lethal effect on *Micrococcus pyogenes* var. *aureus* and *Streptococcus faecalis* as is needed to produce a bacteriostatic effect, and 10–16 times as much is needed to kill saprophytic mycobacteria.

Upon repeated subculture *in vitro* of certain strains of staphylococci and streptococci in the presence of increasing concentrations of carbomycin or erythromycin, resistance to either antibiotic and cross resistance between them can be observed (11). However, the appearance of microbial resistance to carbomycin or erythromycin takes place in a gradual step-wise fashion characteristic of penicillin (*q.v.*) and unlike streptomycin (14).

Staphylococci, particularly those resistant to penicillin, and enterococci are sensi-

tive to carbomycin at low concentrations. A group of 34 cultures isolated from resistant clinical cases was studied with respect to the minimum inhibiting concentrations of carbomycin and seven commercially available antibiotics. Little or no cross resistance between carbomycin and the other antibiotics was displayed. Sensitivity of these microorganisms to carbomycin ranged from 0.39  $\gamma$ /ml. to 6.25  $\gamma$ /ml.

The ability of carbomycin to protect mice against a variety of experimental infections caused by microorganisms such as *M. pyogenes* var. *aureus*, *Streptococcus pyogenes*, and *Diplococcus pneumoniae*, has been amply demonstrated (6). Certain protozoa are also found to be sensitive to carbomycin (20,21). In addition, carbomycin possesses effective inhibitory activity against rickettsiae and the larger viruses, as demonstrated *in ovo* and by survival of treated mice and guinea pigs infected with Rocky Mountain spotted fever, psittacosis, rickettsialpox, and scrub and epidemic typhus (26).

### Pharmacological Properties

Carbomycin and carbomycin B have a low order of toxicity in experimental animals. Carbomycin has an oral LD<sub>50</sub> of greater than 3500 mg./kg. in mice and 6000 mg./kg. in rats. Chronic human studies (24) on four subjects given 250 mg. of carbomycin orally every six hours for eight weeks revealed that the drug is well tolerated and shows no evidence of toxicity (17). Nausea and occasional vomiting are the principal side effects.

Daily intravenous injection of carbomycin (13) at a level of 200 mg./kg. for five days was tolerated well by dogs. There was no alteration in the nonprotein nitrogen. Daily oral or intramuscular administration of carbomycin at the same level for as long as 20 weeks produced no untoward systemic symptoms in dogs. Further confirmation of the safety of carbomycin was obtained from an experiment in which rats grew at a rate indistinguishable from controls when they were fed as high as 0.4% carbomycin in the diet for as long as 17 weeks. Carbomycin did not sensitize guinea pigs. Moreover, cats receiving daily intramuscular injections of 200 mg. of carbomycin per kilogram for nine weeks showed no evidence of eighth cranial nerve damage, which contrasts the nontoxicity of this compound with streptomycin and dihydrostreptomycin. No other significant pharmacodynamic effects such as that on the spontaneous activity of isolated rabbit ileum have been detected; the antibiotic does not affect the response of the ileum to epinephrine, acetylcholine, or histamine. In anesthetized cats, slow intravenous injection of carbomycin hydrochloride at a concentration up to 100 mg./kg. did not cause any significant change in blood pressure.

Detectable levels of carbomycin can be found in rabbit serum within 0.5 hour after the administration of a single intramuscular dose of carbomycin hydrochloride or sulfate (4). When carbomycin hydrochloride or sulfate is given orally to the rabbit, a somewhat lower serum concentration results during this same period. The intravenous administration of carbomycin hydrochloride, however, results in immediate high serum concentrations. Clinicians have observed, upon the treatment of patients by either the oral or the intramuscular route, significant blood levels of carbomycin for as long as four hours (16).

Studies on the distribution of carbomycin (7) in the rabbit after a single dose, either by the oral or intravenous routes, reveal it in all tissues except brain and muscle in concentrations ranging from 1 to 10  $\gamma$ /g. at the end of three to four hours. After

the same time, from 20 to 70  $\gamma$ /ml. is found in the contents at various sites in the gastrointestinal tract; the urine contains as much as 300  $\gamma$ /ml. and the bile somewhat more. Only 35–40% of carbomycin administered to the rabbit can be accounted for by antibiotic excreted in urine and faeces.

**Administration and Dosage.** Carbomycin (free base) is available in tablets for oral administration. In adults the usual total daily dose should be 2 g. given in divided doses every six hours. Duration of treatment is best guided by clinical response.

### Specifications and Assay

To meet certain rigid requirements which satisfy the Food and Drug Administration and the medical profession, carbomycin is subjected to various chemical and biological tests of which a few are solubility analyses, paper chromatograms, ultraviolet and infrared spectra, solubility, pH, heavy metal analyses, residue on ignition, toxicity, and microbiological assay.

Carbomycin is subjected to three independent assays before it is marketed. The microbiological assay is carried out by a plate assay method similar to that used for streptomycin (see p. 78) (8). *B. subtilis* (A.T.C.C. 6633) is used as the test organism, and pure carbomycin base as the standard. In addition, the antibiotic is subjected to polariscopic and titrimetric determinations for potency.

### Indications and Uses

Carbomycin is indicated in the treatment of infections caused by Gram-positive bacteria such as staphylococci, pneumococci, hemolytic streptococci, and enterococci which prove resistant to penicillin or other antibiotics and in the treatment of infections caused by these organisms in patients who have a hypersensitivity to penicillin or other antibiotics. Among the clinical indications for carbomycin are pneumonia, urinary tract infections, soft tissue infections, abscesses, pharyngitis, tonsillitis, and laryngitis. Based on a series of cases of pneumococcal pneumonia, carbomycin was found to be less effective than "broad-spectrum" antibiotics (10); however, in another series of similar infections the drug appeared satisfactory and efficacious (9).

Several investigators have demonstrated that carbomycin is a very efficacious drug in the treatment of acute and chronic amebiasis (14). Most of these patients showed, during an observation period, stool examinations which were negative for *Endamoeba histolytica*.

Carbomycin has been found to be active against the agent of air sac disease of poultry (chronic respiratory disease) *in ovo*. Preliminary tests in infected flocks of chickens confirm its effectiveness (25).

### Bibliography

- (1) Bartholomew, W. H., Karow, E. O., Sfat, M. R., and Wilhelm, R. H., *Ind. Eng. Chem.*, **42**, 1801 (1950).
- (2) Brown, W. E., and Peterson, W. H., *Ind. Eng. Chem.*, **42**, 1769 (1950).
- (3) Demerec, M., *J. Clin. Invest.*, **28**, 891 (1949).
- (4) English, A. R., Field, M. F., Reilly, J., McNierney, J., and Pan, S. Y., *Antibiotics and Chemotherapy*, **3**, 307 (1953).
- (5) English, A. R., Field, M. F., Szendy, S. R., Tagliani, N. J., and Fitts, R. A., *Antibiotics and Chemotherapy*, **2**, 678 (1952).

- (6) English, A. R., Mullady, H. E., and Fitts, R. A., *Antibiotics and Chemotherapy*, **3**, 94 (1953).
- (7) English, A. R., Rapuzzi, L., Field, M. F., McNierney, J., and Pan, S. Y., *Antibiotics Annual, 1953-1954*, 522.
- (8) *Federal Register*, **17**, 6579 (1952).
- (9) Field, W. W., and Taylor, C., *Antibiotics and Chemotherapy*, **4**, 65 (1954).
- (10) Finland, M., Purcell, E. M., Wright, S. S., and Del Love, B., Jr., *New Engl. J. Med.*, **249**, 310 (1953).
- (11) Finland, M., Wilcox, C., Wright, S. S., and Purcell, E. M., *Proc. Soc. Exptl. Biol. and Med.*, **81**, 725 (1952).
- (12) Finlay, A., and Regna, P. P., *Proc. VIIth Intern. Congr. Microbiology, Rome, Sept. 1953*, p. 58.
- (13) Gardocki, J. F., Pan, S. Y., Rapuzzi, A. L., Fanelli, G. M., and Timmms, W. K., *Antibiotics and Chemotherapy*, **3**, 55 (1953).
- (14) Hewitt, W. L., and Wood, J. P., *New Engl. J. Med.*, **249**, 261 (1953).
- (15) Hochstein, F. A., Murai, K., and Regna, P. P., *J. Am. Chem. Soc.* (in press).
- (16) Morgan, G. E., *Harlem Hospital Bull.* **6**, 84 (1953).
- (17) Musselman, M., and Caffery, E. L., unpublished data.
- (18) Regna, P. P., Hochstein, F. A., Wagner, R. L., and Woodward, R. B., *J. Am. Chem. Soc.*, **75**, 4625 (1953).
- (19) Sodeman, W., and Jung, R. C., *J. Louisiana State Med. Soc.*, **105**, 171 (1953).
- (20) Seneca, H., *Southern Med. J.* (in press).
- (21) Seneca, H., and Ides, D., *Antibiotics and Chemotherapy*, **3**, 117 (1953).
- (22) Tanner, F. W., English, A. R., Lees, T. M., and Routien, J. B., *Antibiotics and Chemotherapy*, **2**, 441 (1952).
- (23) Wagner, R. L., Hochstein, F. A., Murai, K., Messina, N., and Regna, P. P., *J. Am. Chem. Soc.*, **75**, 4684 (1953).
- (24) Wiasbren, B. A., Musselman, M. M., DeCamp, P. T., Longacre, A. B., Lattimer, J. K., Katz, S., and Kagan, B. M., unpublished data.
- (25) Wong, S. C., and James, C. G., *Poultry Sci.*, **32**, 589 (1953).
- (26) Wong, S. C., James, C. G., and Finlay, A., *Antibiotics and Chemotherapy*, **3**, 741 (1953).

PETER P. REGNA AND A. C. FINLAY

## VIOMYCIN

Viomycin (Viocin, Vinaetin) is an antibiotic produced by a group of closely related strains of actinomycetes: *Streptomyces vinaceus* (*Actinomyces vinaceus*) (31), *Streptomyces puniceus* (10) (*Streptomyces californicus* (24)), and *Streptomyces floridus* (9). Two and possibly three antibiotics, designated Vinaetin A, B, and C appear to have been isolated in crude form from the culture broth of *S. vinaceus* (26). Vinaetin A is identical with viomycin (7a,31). The antibiotic is effective against tubercle bacilli including those strains resistant to streptomycin, isoniazid, and *p*-aminosalicylic acid. See also *Tuberculostatic agents*.

### Physical and Chemical Properties

Viomycin is a polyacidic strong base of the empirical formula  $C_{78}H_{91-93}N_9O_8$  (12). The free base has not been prepared, but several stable crystalline salts, such as the sulfate, hydrochloride (2), reineckate, oxalate, sulfate picrate, and picrate (12) have been made. Hydrated viomycin sulfate decomposes at about 280°C. and shows  $[\alpha]_D^{25} - 32^\circ$  ( $c = 1\%$  in water) (10). It is highly soluble in water and virtually insoluble in most organic solvents. The ultraviolet absorption spectrum (2) of the sulfate shows a strong maximum which shifts with change of pH:  $E_{1\text{ cm}}^{1\%}$ , 339 at 268  $m\mu$  (0.1 *N* HCl), 334 at 268.5  $m\mu$  (pH 7), and 219 at 282.5  $m\mu$  (0.1 *N* NaOH).

The antibiotic gives positive Sakaguchi (10), biuret, and ninhydrin tests (2), but the maltol, Molisch, and Benedict tests are negative. Viomycin possesses one primary amino group as indicated by Van Slyke determination, several amino acids bound through peptide linkages, a creatinine group, and a guanidino group. Qualitative tests indicate no free  $\alpha$ -amino carboxy groups, no normal carbohydrate, no carbonyl or phenolic oxygen, and no purine nitrogen. Vinaetin A and B appear to be similar peptides in which guanidino and creatinine groups have been reported to be present. Preliminary indications suggest the presence of creatinine in Vinaetin C.

Upon vigorous acid hydrolysis, there is complete microbiological inactivation. Chromatograms of vigorous acid hydrolyzates of Vinaetin A showed evidence of serine, lysine, alanine, and glycine as well as glutamic and aspartic acids (26). Products of the acid hydrolysis of viomycin (12) are L-serine,  $\beta$ -lysine ( $\beta,\epsilon$ -diaminocaproic acid, 3,6-diaminohexanoic acid, identical with the diaminohexanoic acid isolated from streptothricin (4) and streptolin (29)),  $\alpha,\beta$ -diaminopropionic acid, urea, carbon dioxide, ammonia, and an unidentified guanidino component of approximate formula  $C_5H_{10}N_3$  (12).

### Preparation and Manufacture

Organisms that produce viomycin may be preserved by lyophilization (5). Spores are produced in 7–14 days when *S. vinaceus* is grown on nutrient agar slants containing a small amount of yeast extract or on a glucose-peptone-mineral salts agar. Such spores are used to produce larger amounts of vegetative inoculum by seeding tanks containing a medium composed of a source of carbohydrate, such as dextrose, maltose, glycerol, or beet molasses; a source of nitrogen, such as soybean meal, casein, casein hydrolyzate, corn steep liquor, or wheat gluten; a source of growth factors, such as yeast extract, distiller's solubles, or cane molasses fermentation residues; 0.5% sodium chloride and other mineral salts; and sufficient calcium carbonate to maintain the pH at 6.5. A temperature of 27–28°C. for about 24 hr. is found most appropriate for growth.

A similar medium used for the actual fermentation is inoculated with 2–5% of preformed vegetative mycelium as described above. Both the inoculum and fermentation media are sterilized by maintaining a temperature of 121°C. from 10 to 60 minutes depending upon the size and type of equipment. In general, equipment which is suitable for the penicillin fermentation with respect to agitation and aeration, is found satisfactory for both the inoculum and fermentation stages (1,3). The course of the fermentation is followed by the rise in pH to 7.5, mycelium weight, and potency determinations. The potency of fermentation broths is determined by a four-fold *Escherichia coli* serial dilution assay (19). When the true viomycin potency has attained its maximum, generally at about 48–60 hours, the fermentation is halted. Potencies as high as 650  $\gamma$ /ml. of viomycin have been obtained (5) when 100 ml. broth in 500-ml. Erlenmeyer flasks was shaken on a rotary shaker (6-in. circle, 160 r.p.m.) at 24–26°C. for five days. By quiet surface growth, maximum activity against *Mycobacterium tuberculosis* var. *hominis* is produced within 25–30 days (31).

Recovery of viomycin from the broth (31) is accomplished by adsorption on activated charcoal, elution by dilute acid, and repeated chromatography on alumina. In this way 60 mg. of viomycin hydrochloride is recovered from each liter of filtered broth.

The antibiotic may also be recovered by separating the mycelium from the broth by filtration after adjustment to pH 3 with hydrochloric acid. The pH may then be adjusted to about 8 with sodium hydroxide and the broth adsorbed on columns of ion exchange resin, for example Amberlite IRC50. Viomycin base is retained on the resin, impurities are washed out by water, and the resin is then eluted with hydrochloric acid to pH 2.0. Crystalline viomycin hydrochloride can be obtained from the eluate after vacuum evacuation.

A third recovery procedure consists of precipitation of the antibiotic from broths, previously freed from mycelium, with various dyes, such as Erio Chrome Violet BA (20). The dye salt is converted to viomycin sulfate in the presence of organic solvents and triethylamine sulfate. After some degree of refinement during recovery procedure, the activity of preparations may be followed by a plate assay using *Klebsiella pneumoniae* as the assay organism (18).

Viomycin is produced by Chas. Pfizer & Co., Ciba Pharmaceutical Products, Inc., and Parke, Davis and Co. It is sold as the sulfate in the form of a sterile powder, which is easily dissolved in sterile pyrogen-free water for intramuscular injection. Viomycin sulfate in the dry form may be stored at room temperature for 24 months without appreciable loss of potency. Solutions of viomycin sulfate at pH 5-6 may be stored at room temperature under sterile conditions for one week without significant loss. For longer periods of time, a temperature of 5°C. is recommended. At 100°C., the half life of such solutions is approximately 12 hours.

### Microbiological Properties

Viomycin is bacteriostatic and like streptomycin rarely exerts a bactericidal effect. It further resembles streptomycin in the pattern in which resistance develops (9). Cross-resistance does not appear to occur between viomycin and streptomycin, or isoniazid (13).

Viomycin is highly active against *M. tuberculosis*, including strains resistant to streptomycin, neomycin, isoniazid, and *p*-aminosalicylic acid (13,14,15,25,30). It is also active against Gram-positive and some Gram-negative bacteria but not against the fungi, protozoa, and viruses tested.

Purified viomycin sulfate is bacteriostatic for the virulent human H37Rv strain of *M. tuberculosis* var. *hominis* at concentrations of 2.5-12.5  $\gamma$ /ml. (9). The effect of viomycin *in vitro* is additive to that of streptomycin and other tuberculostatic agents against the H37Rv strain.

Viomycin by both oral and intramuscular administration is capable of exerting a marked suppressive effect on tuberculous infections in experimentally inoculated mice (14) and in guinea pigs (15,16,25). In the group infected with streptomycin-sensitive tubercle bacilli, the effect of administering viomycin was comparable to that produced by treatment with streptomycin. The streptomycin-sensitive infection and the streptomycin-resistant infection appeared to be equally affected by the administration of viomycin.

Viomycin, even in high doses, failed to protect mice against experimental infections due to *Streptococcus pyogenes* (*S. hemolyticus*), *Diplococcus pneumoniae*, or *Pseudomonas aeruginosa* (*P. pyocyanea*), but showed definite chemotherapeutic activity against *Klebsiella pneumoniae*, *Salmonella typhosa*, and *Proteus vulgaris* under comparable conditions. Viomycin was effective against these organisms when administered orally as well as subcutaneously, provided a sufficiently large dose was used.

### Pharmacological Properties

**Toxicity.** Viomycin has a relatively low toxicity (14,21); in all instances given here "viomycin" refers to the sulfate. The acute intravenous  $LD_0$  of viomycin for the mouse was found to be 120 mg./kg., while its acute intravenous  $LD_{50}$  is 165–240 mg./kg. The acute subcutaneous  $LD_{50}$  of viomycin in mice is given as 1380 mg./kg. Slow intravenous injections of 100 mg./kg. to anesthetized cats or dogs caused no appreciable drop in blood pressure. When dosages of 120–210 mg./kg. of pure viomycin were administered subcutaneously to mice, once or twice daily for periods of five days, no toxicity was observed. For the rat, subcutaneous administration of 120–360 mg./kg./day for 3–5 days gave no indication of renal damage.

Further studies of viomycin in experimental animals have shown no toxicity in rats, dogs, cats, or other species of animals with dosages equivalent to 50 mg./kg. or less of viomycin administered daily for prolonged periods. No ill effects were demonstrated in rats given daily subcutaneous injections of 50–100 mg./kg. viomycin over a period of six weeks. Daily intramuscular injections of viomycin of 50–100 mg./kg. were tolerated by dogs for a period of more than 150 days. However, disturbances of posture and gait were observed in cats receiving daily intramuscular injections of viomycin of 50–100 mg./kg. These disturbances appeared in 25–33 days with the larger dose and 34–45 days with the smaller dose.

A solution of viomycin is nonirritating. In animals, a 10% solution can be given subcutaneously, intramuscularly, or intravenously without causing local pain, necrosis, or thrombophlebitis.

The pharmacologic study of viomycin in humans has been reviewed carefully in order to determine the potential toxicity of this antituberculous agent when used in high daily doses over prolonged periods of time (11,23,28). Viomycin showed a certain amount of toxicity when administered intramuscularly daily in rather high doses. However, lower, intermittent dosage regimens, alone (2 grams daily over a period of time not exceeding a month or 2 grams every third day for more prolonged periods) and in combination with other antituberculous agents, revealed only minor transient toxic reactions (13) such as allergic reactions or disturbances in the serum electrolyte pattern. These two reactions can generally be alleviated by the administration of antihistamine drugs or supplemental potassium chloride, respectively.

**Absorption and Excretion.** Viomycin is absorbed readily following parenteral administration (14). Following intramuscular administration of viomycin in humans (27), maximum serum concentration of 82–125  $\gamma$ /ml. were attained within two hours after a single dose of 25–50 mg./kg. of body weight. A small proportion of viomycin present in the blood serum appears to diffuse into spinal fluid, pleural, and peritoneal cavities. It is excreted largely by the kidneys; more than 65% of the administered dose can be recovered in the urine within 24 hours. In patients with pulmonary tuberculosis, single intramuscular injections of either 0.1 or 0.5 gram of viomycin sulfate showed that with both dosages the peak plasma levels were attained within one to two hours after the drug had been administered (7).

**Administration.** Viomycin is ordinarily administered by the intramuscular route. The intravenous and oral routes must not be used since the drug causes certain toxic reactions when given intravenously and is not well absorbed from the gastrointestinal tract. The susceptibility of the pathogenic organism to viomycin, the nature and severity of the infection, and the clinical response of the patient are important in determining the dosage of viomycin.

Viomycin is most effective when used in combination with other microbial agents. The recommended dose for most forms of tuberculosis is 2 grams administered intramuscularly in two divided doses at 12 hour intervals every third day alone or in combination with other antituberculous agents such as *p*-aminosalicylic acid (12 grams daily by the oral route), or isoniazid (300 milligrams daily by the oral route). It is recommended that daily administration of viomycin should not exceed 2 grams and should not be continued for more than one month.

The level of drug resistance of microorganisms has not been defined as yet, but it is believed that the incidence and rate of emergence of such resistance may be minimized by the use of combined therapy.

### Specifications and Assay

Like most drugs, viomycin must meet certain rigid requirements that satisfy the Food and Drug Administration and the medical profession. The white crystalline antibiotic salt is subjected to various chemical and biological tests, such as sterility, presence of pyrogens, toxicity, histamine content, optical rotation, heavy metals, solubility, ash, and identification by ultraviolet and infrared spectra.

A method (18) for the bioassay of viomycin employs *K. pneumoniae* (PCI 602, A.T.C.C. 10031) as the assay organism and an incubation period of 3.5 hours. The procedure is essentially that used in the bioassay of the broad spectrum antibiotics (17). This method has been applied successfully on both impure and purified preparations of viomycin. In addition, a paper chromatographic test for identity is employed which is correlated with the bioassay (6,22). A plate assay method using *Mycobacterium butyricum* or *Bacillus subtilis* has also been described (8).

### Indications and Uses

Viomycin appears to be a valuable adjunct in the treatment of the following forms of tuberculosis: progressive exudative, hematogenous lesions and the pneumonic type of pulmonary tuberculosis; cutaneous lesions and fistulas; lymphadenitis; tracheo-bronchial and laryngeal tuberculosis; alimentary, peritoneal, genito-urinary, meningeal, miliary, and bone and joint tuberculosis; and postoperatively in thoracic surgery. Prophylactically it is useful in operations such as lobectomy and pneumonectomy.

### Bibliography for Viomycin

- (1) Bartholomew, W. H., Karow, E. O., Sfat, M. R., and Wilhelm, R. H., *Ind. Eng. Chem.*, **42**, 1801 (1950).
- (2) Bartz, Q. R., Ehrlich, J., Mold, J. D., Penner, M. A., and Smith, R. M., *Am. Rev. Tuberc.*, **63**, 4 (1951).
- (3) Brown, W. E., and Peterson, W. H., *Ind. Eng. Chem.*, **42**, 1769 (1950).
- (4) Carter, H. E., Hearn, W. R., Lausford, E. M., Jr., Page, A. C., Jr., Salzman, N. P., Shapiro, D., and Taylor, W. R., *J. Am. Chem. Soc.*, **74**, 3704 (1952).
- (5) Coffey, G. L., Oyaas, J. E., and Ehrlich, J., *Antibiotics & Chemotherapy*, **1**, 203 (1951).
- (6) Davisson, J. W., Solomons, I. A., and Lees, T. M., *Antibiotics & Chemotherapy*, **2**, 460 (1952).
- (7) Dye, W. E., and Bull, W. F., *Am. J. Clin. Pathol.*, **23**, 56 (1953).
- (7a) Eisman, P. C., personal communication.
- (8) Ehrlich, J., Iverson, W. P., and Kohberger, D., *Antibiotics & Chemotherapy*, **1**, 211 (1951).
- (9) Ehrlich, J., Smith, R. M., Penner, M. A., Anderson, L. E., and Bratton, A. C., Jr., *Am. Rev. Tuberc.*, **63**, 7 (1951).



- (10) Finlay, A. C., Hobby, G. L., Hochstein, F., Lees, T. M., Lenert, T. F., Means, J. A., P'an, S. Y., Regna, P. P., Routien, J. B., Sobin, B. A., Tate, K. B., and Kane, J. H., *Am. Rev. Tuberc.*, **63**, 1 (1951).
- (11) Hackney, R. L., King, E. Q., Marshall, E. E., Harden, K. A., and Payne, H. M., *Diseases of the Chest*, **24**, 591 (1953).
- (12) Haskell, T. H., Fusari, S. A., Frohardt, R. P., and Bartz, Q. R., *J. Am. Chem. Soc.*, **74**, 599 (1952).
- (13) Hobby, G. L., Transactions of the 12th Conference on the Chemotherapy of Tuberculosis held under the auspices of the U.S. Veterans Administration, Army and Navy, Feb. 8-11, 1953, p. 300.
- (14) Hobby, G. L., Lenert, T. F., Donikian, M., and Pikula, D., *Am. Rev. Tuberc.*, **63**, 17 (1951).
- (15) Karlson, A. G., and Gainer, J. H., *Am. Rev. Tuberc.*, **63**, 36 (1951).
- (16) Karlson, A. G., and Gainer, J. H., *Proc. Staff Meetings Mayo Clinic*, **26**, 53 (1951).
- (17) Kersey, R. C., *J. Am. Pharm. Assoc., Sci. Ed.*, **39**, 252 (1950).
- (18) Kersey, R. C., *Antibiotics & Chemotherapy*, **1**, 173 (1951).
- (19) Kersey, R. C., and Fink, F. C., in *Methods of Biochemical Analysis*, Vol. I, Interscience, N.Y., 1954, p. 76.
- (20) Kuehl, F. A., Peck, R. L., Walti, A., and Folkers, D., *Science*, **102**, 34 (1945).
- (21) P'an, S. Y., Halley, T. V., Reilly, J. C., and Pekich, A. M., *Am. Rev. Tuberc.*, **63**, 44 (1951).
- (22) Peterson, D. H., and Reineke, L. M., *J. Am. Chem. Soc.*, **72**, 3598 (1950).
- (23) Pitts, F. W., O'Dell, E. T., Fitzpatrick, M. J., Dye, W. E., Hughes, F. J., Jr., and Tempel, C. W., *Diseases of the Chest*, **23**, 241 (1953).
- (24) Routien, J. B., and Hoffmann, A., *Antibióticos y Quimioterápicos*, **1**, 387 (1951).
- (25) Stenken, W., Jr., and Wolinsky, E., *Am. Rev. Tuberc.*, **63**, 30 (1951).
- (26) Townley, R. W., Mull, R. P., and Scholz, C. R., *Abstracts of the XIIth Internatl. Cong. of Pure and Applied Chem. (New York)*, Sept., 1951, p. 284.
- (27) Werner, C. A., Adams, C., and DuBois, R., *Proc. Soc. Exptl. Biol. Med.*, **76**, 292 (1951).
- (28) Werner, C. A., Tompsett, R., Muschenheim, C., and McDermott, W., *Am. Rev. Tuberc.*, **63**, 49 (1951).
- (29) Van Tamelen, E. E., and Smismán, E. E., *J. Am. Chem. Soc.*, **74**, 3713 (1952).
- (30) Youmans, G. P., and Youmans, A. S., *Am. Rev. Tuberc.*, **63**, 25 (1951).
- (31) U.S. Pat. 2,633,445 (March 31, 1953), W. S. Marsh, R. L. Mayer, R. P. Mull, C. R. Scholz, and R. W. Townley (to Ciba Pharmaceutical Products, Inc.).

A. C. FINLAY AND PETER P. REGNA

**L-STREPTOSE**,  $C_6H_{10}O_5$ . See *Streptomyces antibiotics (streptomycin)*; *Sugars (survey)*.

**STREPTOTHRICIN**,  $C_{13}H_{25}N_5O_7$ . See *Antibiotics*, Vol. 2, pp. 18, 26, 32; *Streptomyces antibiotics (survey)*.

**STRONTIANITE**,  $SrCO_3$ . See *Strontium compounds*.

**STRONTIUM**, Sr. See *Alkaline earth metals*, Vol. 1, p. 463.

## STRONTIUM COMPOUNDS

Strontium forms compounds in which its valence is +2, its compounds resembling those of the other alkaline earth metals (*q.v.*). See also *Barium compounds*; *Calcium compounds*. As a rule, strontium salts are less soluble than those of barium. Strontium salts give a brilliant crimson flame color that is used to detect strontium and in pyrotechnics (*q.v.*). Strontium is determined by weighing as the sulfate after separation from barium (see Vol. 2, p. 308).

Strontium compounds were long confused with those of barium. In 1790 Crawford stated that a mineral believed to be a barium mineral was actually a "new species of earth." This was confirmed in 1792 by Hope. The new mineral, strontianite,  $SrCO_3$ , was so named because it was found in a lead mine at Strontian, Argyleshire, Scotland.

Although many strontium compounds are known, only a few have any industrial importance and are less important than the compounds of the other alkaline earth metals. The principal applications include pyrotechnics, lubricants, driers, and minor applications in medicine. The most important industrial compounds are the peroxide, the hydroxide, the oxide, and the sulfate.

### Occurrence and Production

The chief strontium minerals are celestite,  $\text{SrSO}_4$ , and strontianite,  $\text{SrCO}_3$ . Celestite is used in a modern U.S. process for the production of strontium compounds. Two grades of ore are used: a high-grade ore containing 92%  $\text{SrSO}_4$  and a beneficiated impure celestite, which contains 84–92%  $\text{SrSO}_4$ . The impure ore is first treated with 10% hydrochloric acid, and then with water, thus removing calcium carbonate and a large part of the calcium sulfate, which are the chief impurities. The beneficiated ore, or the high-grade 92% celestite ore, is slowly added to a solution of soda ash at 150–160°F. The solution is contained in wooden reactor tanks equipped with rubber-covered agitators. The solution is agitated for six hours, at the end of which time 80% of the celestite has been converted to strontium carbonate. Part of the supernatant solution is decanted off, more soda ash solution is added, and the solution is agitated for another 10 hours and then is allowed to settle for four hours. The clear supernatant solution is decanted off, and the precipitate of strontium carbonate is washed by decantation three times with hot water. Hydrochloric acid is then added to dissolve the carbonate, and the strontium chloride solution is decanted to a second tank. Here strontium carbonate is reprecipitated by the addition of more soda ash and pumped through a Bird filter. The solids, strontium carbonate plus entrained sodium chloride, are made into a slurry with wash water and washed through a system of 6 Dorr continuous settling and washing tanks. The strontium carbonate from the last tank is dewatered by means of a Bird continuous steel centrifuge, dried in a gas-fired rotary drier, ground in a Micronizer or similar pulverizer, and packaged. Strontium carbonate so prepared (or sometimes naturally occurring strontianite) is the raw material for other strontium compounds.

Celestite can also be reduced, by heating with coke, to the sulfide from which the hydroxide (see p. 116) can be obtained (compare the technology of *Barium compounds*, Vol. 2, p. 308).

### Strontium Acetate.

Strontium acetate,  $\text{Sr}(\text{C}_2\text{H}_3\text{O}_2)_2$ , formula weight 205.72, is a white crystalline salt, soluble in water, 36.4 grams dissolving in 100 ml. of water at 97°C. It crystallizes as the tetrahydrate, or the pentahydrate below 9.5°C. When heated, strontium acetate decomposes. The specific gravity of the anhydrous product is 2.099.

### Strontium Carbonate.

Strontium carbonate,  $\text{SrCO}_3$ , formula weight 147.64, occurs naturally as the mineral *strontianite* in orthorhombic crystals, isomorphous with aragonite,  $\text{CaCO}_3$ , and witherite,  $\text{BaCO}_3$ . The chief locality for its occurrence in the U.S. is at Schoharie, Schoharie County, New York. It is found in commercially important deposits in Westphalia, Germany, and in smaller amounts at many other locations. It is associated with barite,  $\text{BaSO}_4$ , celestite, and calcite,  $\text{CaCO}_3$ , most commonly in veins in marl or

limestone. Strontianite has the following properties: sp.gr. approximately 3.7; Mohs' hardness 3.5; color, colorless to gray or greenish, yellowish, or reddish.

Strontium carbonate is a white crystalline solid, having a rhombic structure below 926°C., the hexagonal above this temperature. It has a specific gravity of 3.70, a melting point (at 60 atmospheres) of 1497°C., and decomposes to the oxide on heating. The "temperature of decomposition" (temperature at which the dissociation pressure of carbon dioxide is one atmosphere) is reported as 1289°C. (4), but published figures vary.

Strontium carbonate is insoluble in water but readily reacts with acids and, like calcium carbonate, will react with and therefore dissolve in carbonic acid. It is also soluble in solutions of ammonium salts. It is sold as a fine white powder of varying grades of purity for the manufacture of other strontium salts. For its manufacture, see p. 114.

**Strontium Cyanide**,  $\text{Sr}(\text{CN})_2$ . See Vol. 4, p. 712.

#### Strontium Formate.

Strontium formate,  $\text{Sr}(\text{CHO}_2)_2$ , formula weight 177.67, m.p. 71.9°C. forms rhombic crystals. It forms a dihydrate which converts to the anhydrous salt at 65°C. It is soluble in water, insoluble in alcohol and ether.

#### Strontium Halides.

**Strontium chloride**,  $\text{SrCl}_2$ , formula weight 158.54, is similar to calcium chloride, but less soluble in water (100.8 grams in 100 ml. water at 100°C.). It forms mono-, di-, and hexahydrates. The anhydrous salt, m.p. 873°C., forms cubic, colorless crystals, with a specific gravity of 3.052. It can be prepared by dissolving the carbonate in hydrochloric acid, concentrating the solution, and crystallizing the salt.

**Strontium bromide**,  $\text{SrBr}_2$ , formula weight 247.46, forms white hygroscopic needlelike crystals, very soluble in water (222.5 grams in 100 ml. water at 100°C.) and soluble in alcohol. A hexahydrate is stable up to 88.6°C., where a dihydrate is formed. The anhydrous salt melts at 643°C. and has a specific gravity of 4.216<sup>24</sup>. It can be prepared by treating the carbonate with hydrobromic acid or bromine in the presence of a reducing agent. Strontium bromide has occasionally been employed as a sedative, instead of sodium or potassium bromides.

**Strontium iodide**,  $\text{SrI}_2$ , formula weight 341.47, forms colorless crystals, which decomposes in moist air. It is very soluble in water (383 grams in 100 ml. water at 100°C.). It forms hexa-, di-, and monohydrates. The anhydrous salt has a specific gravity of 4.549<sup>25</sup>, m.p. 402°C. Strontium iodide can be prepared by treating the carbonate with hydriodic acid. It has been used to some extent in medicine as an alternative for other iodides.

**Strontium fluoride**,  $\text{SrF}_2$ , forms cubic, colorless crystals, or a white powder, sp.gr. 4.24, m.p. 1190°C. It is insoluble in water, but soluble in hot hydrochloric acid. It is isomorphous with fluorite,  $\text{CaF}_2$ .

#### Strontium Nitrate.

Strontium nitrate,  $\text{Sr}(\text{NO}_3)_2$ , formula weight 211.65, exists in the anhydrous form as colorless, cubic crystals, m. p. reported to be 570–645°C. and specific gravity 2.986.

A white monoclinic tetrahydrate,  $\text{Sr}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ , having a density of 2.2 also exists. The anhydrous salt is soluble in water as follows:

Temperature, °C. ....	0	10	20	40	60	80	100
Grams $\text{Sr}(\text{NO}_3)_2$ in 100 g. water. . .	39.5	59.0	68.0	91.3	94.0	97.2	101

The anhydrous salt is the main one produced commercially. Methods reported for making strontium nitrate are by (1) treating strontianite with nitric acid, (2) digesting celestite with soda ash followed by treatment with nitric acid, and (3) heating celestite with coal in a rotary kiln to form a soluble sulfide, followed by treating with nitric acid. Strontium nitrate solutions so formed are purified and a commercial anhydrous strontium nitrate crystal of high purity is prepared by crystallization.

The main use for strontium nitrate is for producing red colors in pyrotechnics (*q.v.*) and railroad fuses. An allied use for strontium nitrate is in tracer bullet compositions. In these uses a high degree of purity is required.

### Strontium Oxides and Hydroxides.

**Strontium oxide**,  $\text{SrO}$ , formula weight 103.63, is a white powder, similar to calcium and barium oxides, and, like them, having the sodium chloride lattice, and a high melting point (2430°C.). It is prepared from the carbonate by heating with carbon in an electric furnace similarly to the preparation of barium oxide (see Vol. 2, p. 316). Its specific gravity is 4.7. It readily combines with water to form strontium hydroxide. It is used as a source of strontium compounds, especially strontium peroxide.

**Strontium hydroxide**,  $\text{Sr}(\text{OH})_2$ , formula weight, 121.63, is a white deliquescent material; m.p. 375°C.; sp.gr. 3.625. Its solubility in water (3) is greater than that of calcium oxide, being 0.41 gram and 21.83 grams per 100 grams water at 0°C. and 100°C., respectively. The solubility is increased in the presence of ammonium chloride. The octahydrate, colorless tetragonal crystals, sp.gr. 1.90,  $n_D^{20}$  1.499, reverts to the monohydrate on standing in dry air, and on heating to 100°C. to the anhydrous form, which on further heating decomposes to the oxide. Solutions of strontium hydroxide are alkaline and absorb carbon dioxide readily, forming strontium carbonate, or bicarbonate with excess  $\text{CO}_2$ .

Strontium hydroxide forms soaps and greases with a number of organic acids. Insoluble complexes are formed by the interaction of strontium hydroxide with polyhydroxy compounds such as sucrose and glycerol. The hydroxide can also be used to prepare other strontium salts.

The commercial product,  $\text{Sr}(\text{OH})_2 \cdot 8\text{H}_2\text{O}$ , is made by coke reduction of celestite to the water-soluble sulfide. On the addition of caustic soda, crystallization of the hydroxide occurs on cooling. After recrystallization, the crystals are dried to the octahydrate equivalent and packaged in wooden slack barrels.

In another commercial method of preparation, celestite is converted to strontium carbonate (see p. 114) which is then converted to the chloride with hydrochloric acid. Addition of caustic soda yields the crystalline hydroxide (4).

Production of strontium hydroxide in the U.S. is estimated to be between 25 and 50 tons a year. It is currently available at 28¢ per pound for the technical grade.

The commercial grade contains 95% or more strontium hydroxide octahydrate; 0.5–2.5% strontium carbonate and 1.5–5.0% barium hydroxide octahydrate are typically present. The bulk density is 50–60 lb. per cubic foot. It is shipped in 400 lb. net wooden slack barrels.

The strontium greases produced from strontium hydroxide and various soap stocks are useful because of their special properties (see *Lubrication*). They are structurally stable and resistant to oxidation and to breakdown over a wide temperature range, resistant to disintegration by water at ordinary or elevated temperature, and resistant to the leaching action of hydrocarbons. They give superior protection against moisture or salt corrosion, and the grease structure shows good stability when subjected to mechanical working (1).

Coal tar, resins, and long-chain aliphatic acids can be treated with strontium hydroxide to form useful stabilizers, such as strontium naphthenate, for many vinyl plastics. See *Driers and metallic soaps*; *Vinyl resins and plastics*.

Strontium hydroxide has been widely used in Europe for beet sugar refining. It forms an insoluble disaccharate which may be separated and refined. Addition of carbon dioxide regenerates the sucrose together with insoluble strontium carbonate. See *Sugar manufacture*.

Strontium hydroxide has been used to improve the drying characteristics of oils and paints.

**Strontium Peroxide,  $\text{SrO}_2$ .** See Vol. 10, pp. 43, 44.

**Strontium Phosphate,  $\text{SrHPO}_4$ .** See Vol. 10, p. 417.

**Strontium Salicylate.** See Vol. 12, p. 55.

### Strontium Sulfate.

Strontium sulfate,  $\text{SrSO}_4$ , formula weight 183.70, forms colorless or white rhombic crystals, sp.gr. 3.96. It decomposes when heated to  $1580^\circ\text{C}$ . It is more soluble in water than barium sulfate and less soluble than calcium sulfate ( $\text{SrSO}_4$ , 0.0113 gram per 100 ml. water at  $0^\circ\text{C}$ .;  $\text{BaSO}_4$ , 0.000336 gram per 100 ml. water at  $30^\circ\text{C}$ .;  $\text{CaSO}_4$ , 0.209 gram per 100 ml. water at  $30^\circ\text{C}$ .). Strontium sulfate can be prepared from celestite by purification, as described on p. 114. Its chief use is as a source of strontium compounds.

Strontium sulfate occurs as *celestite* chiefly in sedimentary rocks where it is associated with other minerals, including sulfur, strontianite, calcite, and gypsum. In the U.S., large lake-bed deposits and massive beds are found in California. Other locations in the U.S. include Maricopa County, Arizona, and western New York. It occurs widely in smaller deposits. Its properties include: sp.gr., approximately 3.97; Mohs' hardness 3-3.5; color, colorless to pale blue. Its use as a source of strontium compounds is described on p. 115.

### Strontium Sulfides.

In addition to strontium sulfide,  $\text{SrS}$ , a tetrasulfide (polysulfide),  $\text{SrS}_4 \cdot 6\text{H}_2\text{O}$ , and the hydrosulfide,  $\text{Sr}(\text{HS})_2$ , are known.

**Strontium sulfide,  $\text{SrS}$ ,** formula weight 119.70, occurs as colorless or light gray cubic crystals or powder, with a sodium chloride lattice, m.p. above  $2000^\circ\text{C}$ ., sp.gr. 3.70. It is practically insoluble in water, but is soluble in acids, with decomposition. If heated with water it decomposes to form the hydrosulfide and the hydroxide. It can be prepared by reduction of the sulfate with carbon. It has some use as a depilatory and in luminous paints.

**Strontium hydrosulfide**,  $\text{Sr}(\text{SH})_2$ , formula weight 153.78, is prepared as described under strontium sulfide. It is soluble in cold water, and decomposes on heating or on boiling with water.

**Strontium tetrasulfide**,  $\text{SrS}_4$ , formula weight 215.90, forms the hydrate  $\text{SrS}_4 \cdot 6\text{H}_2\text{O}$  which occurs as reddish crystals, m.p.  $25^\circ$ , soluble in water and alcohol. The tetrasulfide is prepared by heating the monosulfide with sulfur, leaching, and evaporating the resulting solution *in vacuo* in the cold.

#### **Strontium Sulfite.**

Strontium sulfite,  $\text{SrSO}_3$ , formula weight 167.70, forms colorless crystals, practically insoluble in water but soluble in alcohol and very soluble in sulfurous acid. It decomposes on heating to give sulfur dioxide.

#### **Bibliography**

- (1) *Chem. & Met. Eng.*, **53** [1], 152-155 (1946).
- (2) Cimelin, 7th ed., System-Nummern 29.
- (3) Mellor, Vol. III, 1926, p. 678.
- (4) Sidgwick, N. V., *Chemical Elements and Their Compounds*, Vol. I, Oxford, 1950.
- (5) Worth, H. J., and McClennon, L. W., *Oil Gas J.*, **45**, [43], 74 (1948).

LOUIS PREISMAN

DESMOND M. C. REILLY (Strontium Hydroxide)

**STROPHANTHIN; STROPHANTHUS.** See *Cardiovascular agents*, Vol. **3**, pp. 214, 216, 218.

**STRYCHNINE**,  $\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_2$ . See *Alkaloids*, Vol. **1**, p. 498; *Cardiovascular agents*, Vol. **3**, p. 223; *Poisons, economic*, Vol. **10**, p. 872; *Stimulants and depressants of the nervous system*, Vol. **13**, p. 5.

**STUCCO.** See *Calcium compounds (sulfate)*, Vol. **2**, p. 772; *Cement products*, Vol. **3**, p. 441.

**STYPTIC PENCILS.** See *Cosmetics*, Vol. **4**, p. 552.

**STYPTICS.** See *Astringents*, Vol. **2**, p. 205.

**STYRAX.** See *Resins, natural*, Vol. **11**, p. 686.

**STYRAX OIL.** See *Oils, essential*, Vol. **9**, p. 589.

## STYRENE

Styrene (vinylbenzene, phenylethylene, styrol, cinnamene),  $C_6H_5.CH:CH_2$ , formula weight 104.14, is the simplest aromatic hydrocarbon with an unsaturated side chain. It is a colorless, flammable liquid with a characteristic, not unpleasing odor. In addition to undergoing typical olefin reactions, styrene is especially characterized by its ready polymerizability, a result of the enhanced reactivity of the vinyl group occasioned by the activating effect of the electronegative phenyl group. The enormous and continuing growth in industrial demand for, and production of, styrene during and since World War II is almost entirely based on its use in polymerization and copolymerization reactions. The major current commercial uses of styrene are copolymerization with butadiene to make GR-S synthetic rubber, and polymerization to a wide variety of resins and plastics. See *Rubber, synthetic; Styrene resins and plastics*.

Although styrene was first produced in 1831 by the pyrolysis of storax (see Vol. 11, p. 686), and its propensity to polymerize was discovered before the middle of the 19th century, its commercial production in the U.S. did not begin in earnest until 1937, except for an abortive attempt in 1933, discontinuance of which was forced by the inferior qualities of the resulting polymers. Styrene production, still small at the time of the entry of the U.S. into the war in 1941, skyrocketed as a result of the synthetic rubber program, approximating 350 million pounds in 1944. The overall trend since has been one of enormous further increase to approximately twice that quantity in 1954; this trend may be expected to continue for some years.

More recently the methyl homologs of styrene (see p. 141) have begun to assume commercial importance.

### Properties

The important physical properties of styrene are given in Table I (4,13,19). Vapor pressure data from several sources are given in Table II (4,5). The infrared and ultraviolet spectrograms of styrene are given in reference (19).

Monomeric styrene is completely miscible with methanol; ethyl alcohol; acetone; ether; carbon disulfide; aliphatic, alicyclic, and aromatic hydrocarbons; chlorinated hydrocarbons; nitroparaffins; acetic acid; and ethyl acetate. It is soluble in the higher ethers, alcohols, and ketones. It has been indicated that the solubility of styrene in polyhydroxy alcohols, such as the various glycols, is limited; this factor serves as a basis for a patent covering the concentration of styrene from aromatic solutions by selective solvent extraction (25). The monomer is itself a good solvent for many organic materials, including polystyrene and a variety of other polymeric, plastic materials. The solubilities of water in styrene and styrene in water are very limited, being less than 0.1 and 0.05%, respectively, at temperatures up to 40°C.

Heats of hydrogenation (8) and polymerization (18) of styrene are:

Hydrogenation to ethylbenzene:

$$\Delta H(381^\circ K.) = -28,658 \text{ cal./mol}$$

Hydrogenation to ethylcyclohexane:

$$\Delta H(381^\circ K.) = -77,893 \text{ cal./mole}$$

Polymerization:

$$\Delta H(298.16^\circ K.) = -16,68^\circ \pm 16^\circ \text{ cal./mole}$$

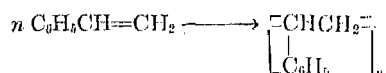
TABLE I. Constants.

Property and condition	Value
B.p. ....	145.2°C.
$dt/dp$ ....	0.049°/mm. Hg
F.p. ....	-30.628°C.
Specific gravity at 20°C. ....	0.90600
$n_D^{20}$ ....	1.54682
Refractivity intercept $n - (d/2)$ , at 20°C. ....	1.09382
Dipole moment, D. ....	0.37 (approx.)
Sp.heat (liquid), at 25°C. ....	0.416 cal./gram)(°C.)
Viscosity at 20°C. ....	0.781 cps.
Surface tension at 20°C. ....	32.2 dynes/cm.
Latent heat of vaporization at 25°C. ....	10,500 $\pm$ 100 cal./mole
Latent heat of fusion ....	2645 cal./mole
Coefficient of expansion at 25°C. ....	0.0009719 cu.cm./°C.
Crit. temp. ....	373°C.
Crit. pressure. ....	40.0 atm.
Volume shrinkage on polymerization ....	17%
Ignition temperature in air. ....	490°C.
Flash point (Cleveland open cup) ....	31°C.
Fire point (Cleveland open cup) ....	34°C.
Explosive limit, lower, in air, at 29.3°C. ....	1.1 vol. %
Explosive limit, upper, in air, at 65.2°C. ....	6.1 vol. %

TABLE II. Vapor Pressure Data for Styrene.

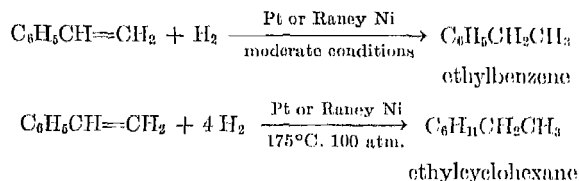
Temp., °C.	Pressure, mm. Hg	Temp., °C.	Pressure, mm. Hg
-20.8. ....	0.185	-40.0. ....	14.51
-13.6. ....	0.38	60.0. ....	39.07
-1.5. ....	1.03	80.0. ....	91.73
10.0. ....	2.34	100.0. ....	192.91
20.0. ....	4.53	120.0. ....	370.67
30.0. ....	8.31	140.0. ....	661.90

**Reactions (9,22).** By far the most important chemical reaction of styrene is polymerization, including copolymerization with other monomers:

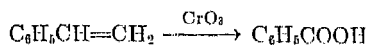


Polymerization is induced by heat or by peroxide or free radical-forming catalysts, or by ionic or acid-acting catalysts of the Friedel-Crafts type.

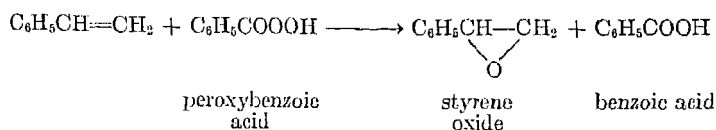
Styrene may be reduced partially or wholly:



The vinyl side chain is readily oxidized, the end products depending on conditions:

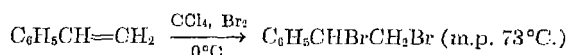




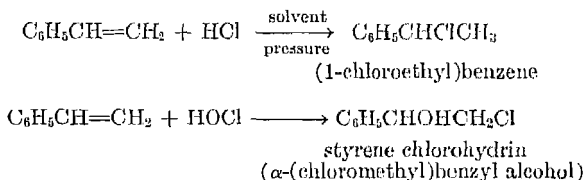


Oxidation with peroxybenzoic acid is reported to give yields of over 70% of styrene oxide (see Vol. 5, p. 923). Air oxidation of styrene gives a mixture of products including formaldehyde, benzaldehyde, and polymers. Potassium permanganate with dilute alkali oxidizes styrene principally to benzoylformic acid (phenylglyoxylic acid),  $\text{C}_6\text{H}_5\text{COCOCO}(\text{OH})_2$ .

Chlorine, bromine, bromine chloride, and iodine chloride readily add to styrene, but styrene diiodide is not formed. The bromine addition reaction is of qualitative and quantitative importance:

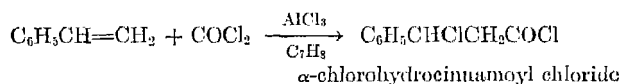


Similarly hydrogen halides and hypohalous acids readily add to styrene:

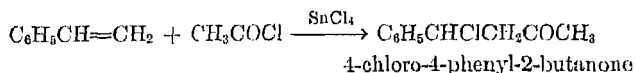


Addition of hydrogen halides normally yields the (1-haloethyl)benzene although, in the presence of lauroyl peroxide, hydrogen bromide adds to give (2-bromoethyl)benzene, showing the typical "peroxide effect."

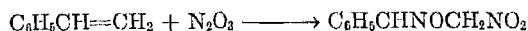
Various oxygen, nitrogen, and sulfur compounds react with styrene. In the presence of aluminum chloride in toluene solution, phosgene reacts:



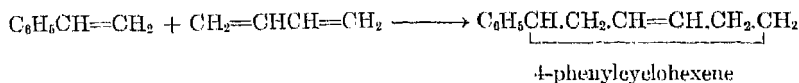
Acetyl chloride addition is catalyzed by stannic chloride:



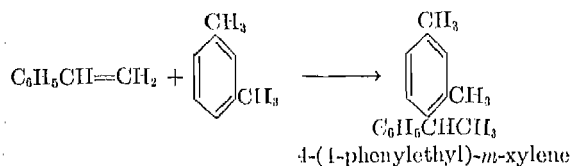
Of a number of addition reactions of organic and inorganic nitrogen compounds, that with nitrogen trioxide is of interest since it has been developed into a quantitative gravimetric analytical method, the probable reaction being (3):



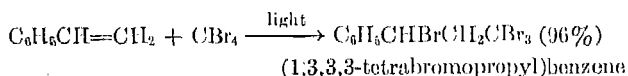
Styrene reacts with hydrocarbons in both the Diels-Alder and Friedel-Crafts reactions. Typical of the former is the reaction with butadiene:



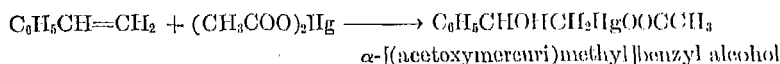
The Friedel-Crafts addition of ArH is typified by the reaction with *m*-xylene:



Among other addition reactions of the vinyl group of styrene are those with polyhalomethanes. The addition of carbon tetrabromide is nearly quantitative:



The reaction of styrene with mercuric acetate is of interest as the basis of a quantitative analytical procedure:



### Manufacture

Although styrene may be prepared in the laboratory by any of a number of processes, only four methods have been used for its production on a commercial scale (22).

- (1) Dehydrogenation of ethylbenzene.
- (2) The acetophenone process, also based on ethylbenzene, but involving the dehydration of  $\alpha$ -phenylethyl alcohol produced by oxidation (see p. 134).
- (3) Pyrolysis of petroleum (see p. 136).
- (4) Recovery from by-products (see p. 137).

Of these, only the first two are currently of commercial importance in the U.S., and the first is used for substantially all the commercial production both in the U.S. and in other countries. Ethylbenzene for processes (1) and (2) above is made commercially by the direct catalytic ethylation of benzene with ethylene. Most installations use an aluminum chloride-catalyzed liquid-phase process, but some ethylbenzene is also made by relatively high-temperature vapor-phase alkylation over phosphoric acid or silica-alumina catalysts under pressure. Table III gives the major U.S. styrene producers and their basic process techniques.

TABLE III. Major U.S. Styrene Producers and Basic Process Techniques.

Producer	Ethylbenzene process	Styrene process
Dow Chemical Co.	Liquid phase; $\text{AlCl}_3$	Vapor-phase dehydrogenation
Monsanto Chemical Co.	Liquid phase; $\text{AlCl}_3$	Vapor-phase dehydrogenation
Koppers Co.	Vapor-phase catalysis	Vapor-phase dehydrogenation
Foster Grant	Liquid phase; $\text{AlCl}_3$	Vapor-phase dehydrogenation
Carbide and Carbon	Liquid phase; $\text{AlCl}_3$	Oxidation-dehydration

Various industrial companies had done pilot plant or laboratory work on the production of styrene before the start of World War II, but the only company in actual commercial production in 1941 was the Dow Chemical Co. Because of the pooling of technical knowledge and efforts, the experience of the Dow company was heavily

relied upon in the national emergency, and the first three companies listed adopted the Dow process in whole or in part for the production of about 90% of the styrene manufactured in this country during the war. The original process and its modifications may be collectively referred to as the Dow process or American process. After the war it was disclosed that although it had been developed independently, the German process was remarkably similar in chemistry, equipment, and yield.

In considering details of the technology of styrene manufacture by dehydrogenation it is convenient to treat separately: (1) the ethylbenzene production step (alkylation), (2) the conversion of ethylbenzene to styrene (dehydrogenation), and (3) the separation of the pure monomer (fractionation). These steps are illustrated schematically in Figure 1.

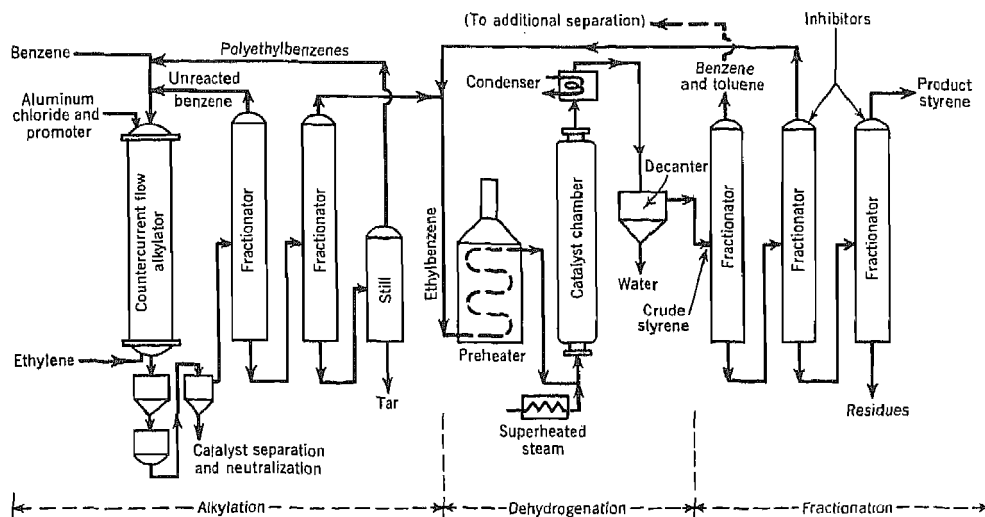
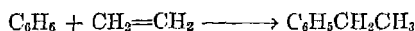


Fig. 1. Flow diagram for styrene monomer production.

### ETHYLBENZENE MANUFACTURE

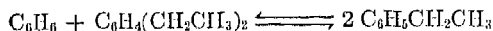
The basic reaction in the Friedel-Crafts alkylation of benzene is:



In practice, the catalytic reaction of benzene and ethylene also produces, as by-products, diethylbenzene and higher polyethylbenzenes. Consequently, processing methods are concerned with the minimization of these more highly ethylated benzenes or their subsequent conversion to the desired monoethylbenzene. The alkylation reaction is exothermic, liberating 1740 B.t.u. per pound of ethylene added; thermodynamically the equilibrium of the reaction shown above lies so far to the right that for all practical purposes all of the ethylene reacts.

**Liquid-Phase Aluminum Chloride Process.** In the more widely used liquid-phase process the alkylation is usually conducted continuously under moderate conditions, typically at about 95°C. and 5 p.s.i.g. reactor pressure, the heat of reaction being removed by condensers from refluxing reactor vapors. Two simultaneous types of reactions actually occur in the reactor. One is the reaction of gaseous ethylene with benzene (and ethylated benzenes) to form the ethyl derivatives. The second is the so-called *dealkylation* or *interchange reaction* wherein polyethylbenzenes react with

benzene to form ethylbenzene. Typical of this second reaction is that of diethylbenzene:



Under appropriate reaction conditions, the first reaction, the absorption of ethylene, is virtually instantaneous, but the interchange reaction is notably less rapid, particularly below about 60°C. Actually, a characteristic equilibrium distribution exists for any mixture of ethyl and phenyl groups, the distribution varying with the molar ratio of ethyls to phenyls, as shown in Table IV. At still higher ratios of ethyl groups the monoethylbenzene percentage decreases again while the polyethylbenzenes steadily increase.

TABLE IV. Equilibrium Distribution in Benzene Ethylation.

Mole ratio, ethyl groups to aromatic groups	Benzene, wt. %	Ethylbenzene, wt. %	Polyethylbenzene, wt. %
0.0	100.0	0.0	0.0
0.2	73.6	21.6	4.8
0.4	52.8	37.6	9.6
0.6	40.6	44.2	15.2
0.8	27.2	50.4	22.4
1.0	18.0	50.8	31.2

It will be seen from Table IV that at about a 1 mole ratio the equilibrium alkylator effluent would contain the maximum weight percentage of ethylbenzene. However, above about a 0.6 ratio the rate of increase in the weight percentage of ethylbenzene is not so great as the rate of increase in polyethylbenzenes, and commercial alkylation units, although they may not produce an exactly equilibrium mixture, normally operate at slightly under a 0.6 ratio. Inasmuch as ethyl groups are supplied both by ethylene and recycled polyethylbenzenes, and phenyl groups are supplied both by benzene and polyethylbenzene, it is necessary to consider all three of these hydrocarbon feeds in calculating reactor mole ratios.

Table V shows the mole percentage of ethylbenzene based on ethyl groups, as a function of the mole ratio of ethyl groups to phenyl groups. As would be expected, the yield of ethylbenzene decreases steadily with increasing mole ratio, theoretically being quantitative at an infinitely small mole ratio. In the reaction of ethylene and benzene alone, it would follow that yields of ethylbenzene at equilibrium would be 90% only at a 0.16:1 ethylene:benzene ratio and 95% at a 0.08:1 ratio. In the recovery of the desired ethylbenzene it would thus be necessary to remove first, by fractionation, a large quantity of benzene per unit of ethylbenzene. Actually, however, because of the interchange reaction referred to, much higher ethylene:benzene ratios are employed and the bulk of the polyethylbenzenes recovered from the reaction product are recycled to the alkylation step to set up a steady-state concentration, giving an overall process yield of ethylbenzene based on ethylene and benzene fed exceeding 95% of theory.

In addition to the anhydrous aluminum chloride, which is normally fed to the top of the tower-type alkylator in solid form, hydrogen chloride is used as a promoter for the reaction. This hydrogen chloride may be added as such, or it may be generated *in situ* by feeding small quantities of water to hydrolyze part of the aluminum chloride. The latter method suffers from disadvantages in the form of increased catalyst con-

TABLE V. Ethylbenzene Yield in Benzene Ethylation.

Mole ratio, ethyl groups to aromatic groups	Ethylbenzene yield, mole % of ethyl groups
0.0.....	100.0 (theoretical)
0.2.....	88.0
0.4.....	76.8
0.6.....	67.2
0.8.....	57.6
1.0.....	51.2

sumption and increased corrosion. Alternatively ethyl chloride may be added, which yields hydrogen chloride under reaction conditions. In American practice the various reagents are carefully dried before use.

The benzene used is known as "styrene grade" and is of high purity. In addition to the fresh, net benzene feed to the alkylator, unreacted benzene recovered by fractionation from the reactor product is continuously recycled, after appropriate drying. Ethylene feedstock is normally of about 95% purity, although this is not absolutely essential. More dilute ethylene, provided the diluents are inert under reactor conditions, suffers from the chief disadvantage of requiring higher operating pressures to prevent undue loss of liquid hydrocarbons. Acetylene is an undesirable impurity, increasing catalyst consumption. When ethyl chloride is used as a promoter, the ethylene feed may be used to vaporize it and carry it into the reactor. The ethylene is fed at the bottom of the tower, in which it flows upward, providing turbulence to aid in mixing the two phases present in the reactor.

The reactor effluent comprises two liquid phases, a large, essentially catalyst-free hydrocarbon layer, and a much smaller, more viscous, higher-density dark layer containing almost all the catalyst. The two layers are cooled and separated, and most of the catalyst complex or sludge layer is returned to the alkylator along with some fresh catalyst. Part of the catalyst complex may be fed to a separate dealkylator where very highly ethylated benzenes are treated at about 200°C. to effect a further conversion to ethylbenzene. A part of the catalyst complex is continuously removed from the reaction system to balance the fresh catalyst fed. As a result of the catalyst recycle, overall aluminum chloride consumption is reduced economically. Although too small a quantity of catalyst results in inadequate ethylene absorption, it is also detrimental to use too much, for then the catalyst complex layer becomes excessive, and by-product formation greater.

The crude reaction product is neutralized with concentrated caustic and the catalyst-free oil is then processed in a series of continuous fractionating stills. Although process details in the recovery process vary, the basic separations are:

- (1) Unreacted benzene, for recycle to the reactor.
- (2) Product ethylbenzene (> 99% pure).
- (3) Polyethylbenzenes (up to about 230–250°C.), for recycle to the reactor.
- (4) Residue, including very highly ethylated benzenes, which may be separately dealkylated in a high-temperature reactor.

The polyethylbenzene recycled to the alkylator for the interchange reaction normally may be expected to contain mainly diethylbenzene along with smaller quantities of tri- and tetraethylbenzenes. In both the American and German processes these

polyethylbenzenes are used to scrub the alkylator vent gases to recover any entrained benzene, ethylbenzene, and hydrogen chloride, and return them to the alkylator. Normally the ethylene content of the vent gases is negligible.

In the fractionation process the ethylbenzene must be carefully freed from diethylbenzene, inasmuch as the latter, in the subsequent dehydrogenation step, yields divinylbenzene which, even in small quantities, is a detrimental impurity in styrene, tending to form insoluble, infusible copolymers. There is danger of the formation of these in the top of the styrene separation columns.

All the aluminum chloride-catalyzed ethylbenzene processes operate on the same basic principles, differing only in details.

*The Dow Process.* In a typical Dow process installation ethyl chloride, vaporized by the ethylene feed, is used to supply the catalyst promoter. Solid anhydrous aluminum chloride is fed to the top of the reaction towers by a mechanical conveyor, which must be protected from atmospheric moisture. The benzene has a purity generally of 99% or better with a minimum freezing point of 4.85°C., a boiling range of 1°C. or less, and a total sulfur content of 0.1% or less. The heat of reaction is removed by reflux condensers at the top of the reactor. The crude product, after partial cooling and separation of the catalyst complex layer, followed by neutralization with 50% aqueous caustic, is first fed to a baffle-plate stripper, wherein benzene, ethylbenzene, and the lighter polyethylbenzenes are separated from smaller amounts of highly polyethylated benzenes and heavy by-products.

The stripper bottoms are fractionated in a 10-plate column at 0.5:1 reflux ratio to separate additional lighter polyethylbenzenes from the heavy residues, which are dealkylated in a separate reactor operating at 200°C. to produce additional benzene and mono- and diethylbenzene which join the alkylator product.

The stripper overheads must be fractionated into benzene, ethylbenzene, and polyethylbenzenes. This is accomplished in a series of two columns. Benzene is separated in a 20-plate column at a 3:1 reflux ratio, ethylbenzene in a 58-plate column at a 3:1 reflux ratio. The polyethylbenzene bottoms, to which are added the overheads from the 10-plate column, are returned to the alkylation tower for the dealkylation or interchange reaction. Before entering the reactor, the polyethylbenzene stream is used as scrubbing oil in an absorption column to remove any entrained ethylene and aromatics from the vent gases from the top of the alkylator.

Ethylbenzene yields from Dow process plants have been reported as averaging 95.5%, based on net benzene fed, and 96.8% based on ethylene. Net aluminum chloride catalyst consumption ranges from 1 to 3 wt. %, based on ethylbenzene produced, the requirements being closely dependent on the type and amount of impurities, including water in the feed materials.

*German (I. G. Farbenindustrie) Process (1).* In the plant at Hüls enameled reaction towers were used and operated at about 90–100°C. Rather similar mole ratios of ethylene to benzene were used to those in the Dow installations. The benzene had a 5.3–5.4°C. freezing point and met tests even more rigid than those required in the U.S. The ethylene was in 94% concentration with < 1% acetylene. Moisture in the ethylene feed was the source of the hydrogen chloride promoter in the reactor. Contact times were such that both ethylation and ethyl group interchange took place in the reaction towers, to which all of the polyethylbenzenes were recycled. The heat of reaction was removed in part by cooling jackets in the upper part of the alkylators and in part by reflux condensers. No separate high-temperature dealkylator was used. About 3% aluminum chloride, based on ethylbenzene, was used.

The reactor effluent was cooled, separated, and the crude ethylbenzene product was freed of residual catalyst by water and caustic washing. Typically, the alkylator effluent was approximately 40% benzene, 38% ethylbenzene, and 22% polyethylbenzenes. The crude product was then processed in a series of four stills to remove overhead benzene for recycle, ethylbenzene product, diethylbenzene, and polyethylbenzene, the bottoms from the last column being tar useful as a plasticizer.

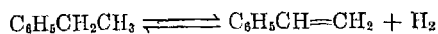
Depending on high-octane gasoline requirements, operations in both the alkylator and the stills could be modified to favor the production of high-purity diethylbenzene. For simultaneous optimum production of mono- and diethylbenzene, the mole ratio in the reactor was increased, by reducing the benzene fed.

In the distillation system, the presence of some ethylbenzene in the recycled benzene is unimportant. However, the purity of the ethylbenzene product is important in the dehydrogenation operations, particularly with regard to freedom from diethylbenzene. Consequently, the second, or ethylbenzene still, had to give a close-boiling overhead ( $< 0.7^{\circ}\text{C}.$ ) essentially free of diethylbenzene. Both benzene and ethylbenzene were normally taken overhead at essentially atmospheric pressure, while higher ethylbenzenes were distilled at reduced pressures. The separations were straightforward and, although requiring careful control, did not pose problems of the complexity of those in the fractionation train used on the dehydrogenated ethylbenzene.

**Vapor-Phase Process.** The Kobuta, Pennsylvania, plant of Koppers was designed for vapor-phase benzene ethylation. Both supported phosphoric acid and silica-alumina catalysts have been used. Such catalysts are less active than aluminum chloride and relatively high reaction temperatures (over  $300^{\circ}\text{C}.$ ) and pressures (exceeding 600 p.s.i.g.) are required. In the vapor-phase process, much lower ratios of ethylene to benzene are used than in the aluminum chloride processes, leading to higher yields of ethylbenzene based on ethylene, at the expense of increasing the amount of unreacted benzene to be separated per unit amount of ethylbenzene produced. This is done because dealkylation or ethyl group interchange of di- and higher ethylbenzenes is very much slower over vapor-phase catalysts than with aluminum chloride and there is a pronounced tendency to deposit on the catalyst bed with a detrimental effect on its activity. For ethylbenzene yields approaching those of the liquid-phase process, ratios of ethylene to benzene of the order of 0.2 have been reported for vapor-phase alkylation. The distillation system requirements for product recovery from the vapor-phase ethylbenzene process are modified in that the reactor effluent contains considerably more benzene and less polyethylbenzenes per unit amount of ethylbenzene produced.

#### DEHYDROGENATION OF ETHYLBENZENE

In 1869, Berthelot obtained styrene by passing the vapors of ethylbenzene through a heated porcelain tube. He also obtained benzene, toluene, and xylene as liquid degradation products. The reversible reaction, which is endothermic, from left to right, is:



The uncatalyzed reaction is perfectly feasible, and it has been reported that one large company was seriously considering installing it on a commercial scale just before World War II. At temperatures around  $600^{\circ}\text{C}.$ , although the theoretical equilibrium

is favorable, the reaction velocity is slow. In order to obtain commercially acceptable conversions per pass, it is necessary to operate at considerably higher temperatures at which the equilibrium is still more favorable, but which result in the formation of excessive amounts of gas and carbon and of liquid by-products, formed by cracking. Since both higher temperatures and longer times of contact favor both the desired dehydrogenation reaction and the undesirable degradation reactions, a compromise is necessary to select a set of conditions favoring a reasonable conversion to styrene per pass as well as a reasonable ultimate yield. Thus, Webb and Corson (23) operating to obtain the maximum yield per pass (without steam) obtained the following results:

Temp., °C.	Contact time, sec.	Styrene yield, %	
		Per pass	Ultimate
700	1.0	21	35
750	0.7	28	48
800	0.1	30	48

By limiting the conditions to give a yield of 20% per pass, and by using steam to reduce the partial pressures, they were able to increase the ultimate yields as follows:

Temp., °C.	Contact time, sec.	Mole ratio, water:ethylbenzene	Ultimate yield at 20% yield per pass
700	0.8	0	38
700	0.8	5	52
750	0.2	0	55
750	0.1	5	60

In the above discussion, the term conversion has been used in the limited sense to denote conversion of ethylbenzene to styrene. The ethylbenzene is also consumed by conversion into other materials, and in the broad sense conversion also covers these. The yield per pass is the product of the liquid recovery (the amount of liquid dehydrogenate per unit of ethylbenzene charged) times the percentage styrene concentration in the dehydrogenate. The net ultimate yield is the yield of styrene per 100 weight parts of ethylbenzene consumed, that is, it is the calculated amount of styrene that would be produced if the ethylbenzene were recycled until it was completely consumed. The ultimate yield can never exceed 98.12%, since this is the theoretical yield of styrene from ethylbenzene. The yields per pass given here, as well as the ultimate yields, are weight yields.

In addition to the use of steam, various other methods have been proposed to favor the progress of the reaction toward the right and improve the yield of styrene. These include operating: (1) under reduced pressure; (2) in the presence of inert diluents; (3) in the presence of hydrogen acceptors to disturb the equilibrium; (4) in the presence of undesirable by-products to suppress their formation; and (5) in the presence of catalysts to obtain a commercially acceptable conversion per pass at temperature levels at which the formation of degradation products is small. Of these and various other proposals, only two—the use of steam and of catalysts—have been employed commercially.

Steam has a number of advantages. In the first place, by reducing the partial pressures, it shifts the equilibrium to the right. In the second place, if the catalyst



promotes the water-gas reaction, steam helps to remove any carbon deposited on the catalyst and thus helps to keep the catalyst activated. Finally, in the American (Dow) process, steam is superheated to a high temperature and thus serves to supply heat to the reactor. It is also claimed that mixing the ethylbenzene with the steam just before contact with the catalyst is an advantage because direct heating of the ethylbenzene in a furnace favors breakdown of this hydrocarbon.

The development of suitable dehydrogenation catalysts is largely responsible for the fact that commercial units obtain ultimate yields of about 90% at styrene concentrations of about 40%. Although a very large number of catalysts have been tried in the laboratory, only a few have achieved importance. They may be divided into two main classes, air-regenerative and steam-regenerative.

A chromium oxide catalyst (about 11–13%  $\text{Cr}_2\text{O}_3$ , 85%  $\text{Al}_2\text{O}_3$ , and 2%  $\text{MgO}$ ) is an example of the air-regenerative type. It is said that this catalyst is poisoned by steam. It is regenerated by passing air over it in a cyclic process, in which the make, purge, and regeneration cycles are controlled by automatic valves.

This type of catalyst is extensively used in the dehydrogenation of butane to butene as the first step in the production of butadiene, but it has never been used commercially for the production of styrene, although it has given good results in the laboratory (15,24) on styrene and excellent results (12) on the production of *p*, $\alpha$ -dimethylstyrene by the dehydrogenation of *p*-cymene. The catalyst may be operated at a very fast throughput, and the production of styrene in pounds per hour per cubic foot of installed capacity would probably be higher than for any steam-regenerative type even with allowance for a regeneration cycle as long as the on-stream cycle (which would be equivalent to having only one of two units on stream at any one time and allowance for one unit in reserve). Apparently, the complexity and hazard of the air-regeneration cycle has been considered to outweigh the advantage of fast throughput.

The steam-regenerative type of catalysts may be subdivided into two classes. The first of these may be operated on a cyclic basis with ethylbenzene and steam present during the make and only steam used during the regeneration cycle. The second class is truly autoregenerative. This type of catalyst is maintained in an active state continuously over long periods of time without any regeneration cycle, although the reaction temperature is raised very slowly to compensate for a slight gradual decrease in activity.

The steam-regenerative type catalyst used in much of the styrene production during World War II was developed by the Standard Oil Co. of New Jersey and was known as 1707 or the "Jersey" catalyst. It was developed primarily for the dehydrogenation of butenes to butadiene in the presence of steam but was widely adopted for the dehydrogenation of ethylbenzene. The composition has been given as 72.4%  $\text{MgO}$ , 18.4%  $\text{Fe}_2\text{O}_3$ , 4.6%  $\text{CuO}$ , and 4.6%  $\text{K}_2\text{O}$  (12).

This catalyst has been largely replaced in the U.S. by catalysts of about 85% iron oxide activated with chromium oxide and promoted with potassium oxide.

Two catalysts were used in Germany, both being largely zinc oxide activated with potassium chromate and sulfate. Their compositions are given in reference (1).

For a given catalyst, the operating conditions chosen are a compromise between relatively mild conditions that give a low conversion per pass with a high ultimate yield, and higher temperatures and longer times of contact that result in higher conversions per pass at the expense of ultimate yield because of an increase in the forma-

tion of benzene and toluene through cracking (dealkylation) and of gaseous by-products and tar. The problem is well illustrated by the following values taken from the paper of Wenner and Dybdal (24), which show the effect of increasing the severity of the dehydrogenation conditions:

Styrene monomer, % by weight in dehydrogenate	Ultimate yield, corrected for perfect recovery
38.2.....	89.5
45.7.....	86.5
56.9.....	81.4

Similar results were obtained in plant tests at H÷ls (1).

Naturally, it is desirable to obtain a high conversion per pass since operating costs per pass are essentially fixed (the steam consumption, for example, is based on the feed, not on the styrene produced), but in practice the economics favors limiting the conversion per pass and increasing the number cycles. In the U.S. the conversion is limited to give slightly under 40% per pass.

Although the German and American processes are similar in many respects, they differ radically in the type of reactor and in the amount of steam used. In the German process (1) the catalyst was maintained in a bundle of parallel tubes heated externally by products of combustion. In some installations the converters had 92 tubes about 4 in. (100 mm.) in diameter and about 10 ft. (3 m.) long. In others, the banks consisted of 26 tubes somewhat over 7 in. (185 mm.) in diameter. The smaller tubes gave better heat transfer but more back pressure. The tubes were of stainless steel with copper manganese liners. They were in the vertical position with the gas flow downward. The heating was by direct gas firing with the products of combustion baffled around the tube banks both vertically and horizontally. Steam and ethylbenzene were preheated in a two-stage heat exchanger with the products of combustion from the furnace and with the reaction gases, bringing them nearly to the reaction temperature.

The steam and ethylbenzene were used in a 1.2-1.5:1 weight ratio (not an equimolecular ratio, as incorrectly reported by the American investigators). With fresh catalyst the temperature was 580°C., this being very gradually raised to 610°C. over a period of about one year. The liquid dehydrogenate had the percentage composition: styrene, 40.0; ethylbenzene, 58.2; benzene, 0.5; toluene, 1.0; and tar, 0.3. The ultimate yield was about 90%.

The American process (4) differs from the German in four respects: (1) The catalyst is maintained in a massive bed instead of in a bundle of tubes. (2) The unit is adiabatic, the necessary heat being supplied by preheating the steam. (3) Because of (2) and possibly partly because of a difference in the catalyst, the steam:ethylbenzene ratio is 2.6:1 by weight or about twice that in the German process. (4) The temperature is slightly higher.

With fresh catalyst, the temperature at the bottom (inlet) of the bed is about 600°C. This is very gradually raised to about 660°C. (4). Taking 630°C. as an average for a long period of operation, the heat is supplied by preheating about 90% of the steam to 710°C. (after heat exchanging it to 385°C.). The other 10% of the steam is mixed with the ethylbenzene before passing through a vaporizer, where the mixture is heated to 160°C. It is then heat-exchanged with the hot reactor gases to a temperature of 520°C. just before it meets the superheated steam which gives it a temperature of 630°C. at the inlet to the catalyst bed, which is the control point. The

product leaves the dehydrogenator at 565°C., being cooled in a two-stage heat exchanger first with the ethylbenzene stream and then with steam. It is then cooled to 105°C. to separate some tar and finally condensed and separated into water and oil phases.

The reactor is a refractory-lined steel shell. The catalyst is held in place by a ram. The ethylbenzene and steam are mixed in a concentric tube. Gas flow is upward, the outlet being screened to prevent loss of catalyst. The ultimate yield is about 90%. The percentage composition of the liquid dehydrogenate is: styrene, 37.0; ethylbenzene, 61.1; benzene, 0.6; toluene, 1.1; and tar, 0.2.

The question whether the German or the American system is the more efficient is a difficult one to answer. Construction costs should be higher for the German tube-bundle system, and the published data show the same ultimate yield but a somewhat higher styrene concentration and a steam consumption of about 3.5 lb./lb. styrene compared to 7.0 lb. for the American system.

Wenner and Dybdal (24) discussed the dehydrogenation of ethylbenzene from the thermodynamic and kinetic point of view. For a massive bed system, a reactor of 4-ft. internal diameter, with an inlet temperature of 625°C., a molar steam:ethylbenzene ratio of 20:1, and a styrene conversion of 45% were assumed. To produce 15 tons of styrene per day, it was calculated that two beds with reactor heights of 5.1 ft. would be required, that the steam consumption would be 7.7 lb./lb. styrene produced, and approximately 9.8 lb. of styrene would be produced per cubic foot of installed catalyst per hour. For a tube-bundle system, tubes of 4.03-in. diameter, a molar steam ratio of 10:1, and 45% conversion were assumed. To produce the same 15 tons of styrene per day, it was calculated that 172 tubes 5.3 ft. long would be required, that the steam consumption would be 3.84 lb./lb. styrene produced, and approximately 15.6 lb. of styrene would be produced per cubic foot of installed catalyst per hour. The latter figure is about 60% higher than the corresponding figure for the massive bed system. The steam consumption is about half as much, but since additional fuel would obviously be required to heat the converter, the total saving in fuel would not be so large as the difference in steam consumption. The calculations appear to favor the tube-bundle over the massive bed system.

#### SEPARATION OF STYRENE

The separation of pure styrene from the crude liquid dehydrogenate requires its separation from benzene, toluene, and tar, which is very easy, and also from ethylbenzene, which might appear to be only moderately difficult, but which in practice proved to be extremely difficult. The difference in boiling points is small (ethylbenzene 136.2°C., styrene 145.2°C., both at 760 mm.), and the propensity of the styrene to polymerize makes it impossible to separate the two by fractionation at atmospheric pressure. When fractionation under reduced pressure was attempted, it was found that the pressure drop of the column required for the separation was so great that the pot temperature was excessive regardless of the overhead temperature and pressure.

Numerous polymerization inhibitors are known that are effective at moderate temperatures, but they lose their effectiveness and may actually become accelerators at higher temperatures. About 90°C. may be taken as the maximum temperature at which concentrated styrenes can safely be heated with an inhibitor in commercial fractionation. In practice, it was found that about 70 actual plates were required for the separation. A pressure drop of 3 mm. per plate would correspond to a pressure

of 210 mm. through the column. With an overhead pressure of 1 mm., this would still correspond to a temperature of slightly over 100°C. in the reboiler.

The published solution to this problem by the Dow company was twofold (4). The column was divided into two parts and sulfur was added as an inhibitor to the reflux. In operation, the crude dehydrogenate is passed through a container containing sulfur and is then fed into the side of a 30-plate column which is operated at 175 mm. and a reflux of 12:1 to remove overhead benzene and toluene, which are subsequently separated in a conventional column. The dissolved sulfur passing down the column effectively inhibits the stripping section.

The bottoms, consisting of ethylbenzene, styrene, tar, and sulfur, are separated into ethylbenzene overhead and styrene bottoms in two columns rather than one. The first, which may be considered to be a primary ethylbenzene column or the top section of a single column, has 38 plates. The second, which may be considered to be a secondary ethylbenzene column, or the lower section of a single column, has 32 plates. Sulfur is added to the ethylbenzene reflux of the primary column. The overhead pressure in each column is maintained at 35 mm., and the maximum bottoms temperature is about 90°C. Precautions are taken to prevent high skin temperatures and to prevent leakage of air into the system.

The overhead from the primary column is ethylbenzene containing about 6% styrene. It is recycled directly to the dehydrogenation unit. The bottoms from this column are pumped through a cooler to the top of the secondary column. The overhead from the secondary column passes through a condenser and then flows by gravity to the reboiler of the primary column. The bottoms from the secondary column consist of a mixture of styrene, sulfur, tar-sulfur compounds, and any polymer formed up to this point. This stream is cooled and fed to a storage tank, which is maintained at 35 mm. pressure.

The finishing operation for the crude styrene bottoms is in batch stills, with 36-ft. columns packed with 2-in. Raschig rings. These columns are operated at 35 mm. pressure with an overhead temperature of 57°C. A solution of T.B.C. (4-*tert*-butylpyrocatechol) is added to the reflux of these columns to inhibit polymer formation in the column above the point at which enough sulfur is present. The bottoms from the finishing columns are burned. The overhead, which is styrene of 99% or greater purity is inhibited with T.B.C. to give a concentration of about 10 p.p.m. The product styrene is cooled to a temperature of less than 21°C. (70°F.) while being loaded into tank cars, which are usually insulated.

The addition of sulfur to the feed to the fractionation system, and particularly to the ethylbenzene reflux, plus the rigid control of the bottoms temperatures throughout the system are the keys to the successful American production of styrene by this method. It is claimed that the on-stream efficiency of the distillation system is more than 95% and that the loss of styrene in the system is only about 0.6% (including polymer and styrene-sulfur compounds). In this connection it should be noted that the economic loss due to the formation of styrene polymer is not the primary cause of concern. Excessive polymer formation with the resulting plugging of columns, lines, and equipment with very difficultly soluble resin would entail very expensive and time-consuming cleaning operations.

The whole American process is highly instrumented. In one plant (Velasco, Texas) there are 960 indicating and recording instruments, exclusive of gages and thermometers.

Obviously, the fractionation system as described is not the only one that would function. A modification of this system is used in the Monsanto plant at Texas City. Benzene, toluene, and ethylbenzene are taken overhead together in the first column and are separated in another series of columns. The bottoms of the primary column are separated into a styrene overhead and a tar residue in a second continuous column. This system permits the concentrated styrene being heated in the reboiler of only one column, but, at least in the initial operations, the temperatures were higher and polymer losses were higher than in the more involved system.

The German still systems for separating styrene differed in several respects from the one described above (1,4). Most important was the use of lower operating pressures, permitting lower temperatures. Hydroquinone was apparently the only inhibitor used, and it was not added to the reflux.

The Hüls still system consisted essentially of three continuous columns, the bottoms from each being fed to the next:

Column	No. of plates	Feed plate	Top of column		Bottom of column		Reflux ratio	Overhead composition
			Mm.	°C.	Mm.	°C.		
1	45	15-21	25-30	40-45	175	100	4:1	Benzene, toluene, ethylbenzene
2	24-28	10-20	15-20	35-40	70-75	80-85	8 or 10:1	40% styrene, 60% ethylbenzene
3	20	10	10	35	40-45	80-85	5:1	99 + % styrene

The overhead from the first column was separated successively in partial and total condensers, the first condensate (relatively pure ethylbenzene containing about 2% styrene) being recycled to the dehydrogenation unit, the benzene and toluene, and the balance of the ethylbenzene, being condensed at about 2°C. and removed from the system for fractionation in separate stills. The overhead from the second column (crude styrene still) was recycled to the feed to the still system. The bottoms from the third column (pure styrene still) contained some styrene which was separated in a small tar still and returned to the feed to the pure styrene still.

At Hüls, three-stage steam ejectors with steam at 4-5 atm. were used to provide the low pressures at which the columns were operated. Provision was made for removal of the lower plates for cleaning, but the stills normally operated 6-9 months without cleaning.

The ethylbenzene used in the dehydrogenation step in the American process has a purity in excess of 99% and met rigid specifications. In Germany it had a sulfur content below 0.2% and had a maximum boiling range (total spread) of 0.5-0.7°C., a total range of 0.2°C. being sometimes obtained. Such close boiling ranges practically exclude toluene, but the exclusion of diethylbenzene is much more important. The Dow specification for diethylbenzene in ethylbenzene is 0.04%. In Germany the purity of the ethylbenzene was very high, the diethylbenzene and toluene at Schkopau being less than 0.002% (4).

Commercial styrene monomer as produced by dehydrogenation is an extremely pure chemical compound which normally assays 99.5% or better. However, the fact that traces of compounds such as phenylacetylene and divinylbenzene have a pronounced influence on polymerization behavior means that the assay is of less importance than the concentrations of these and other compounds. Depending upon the

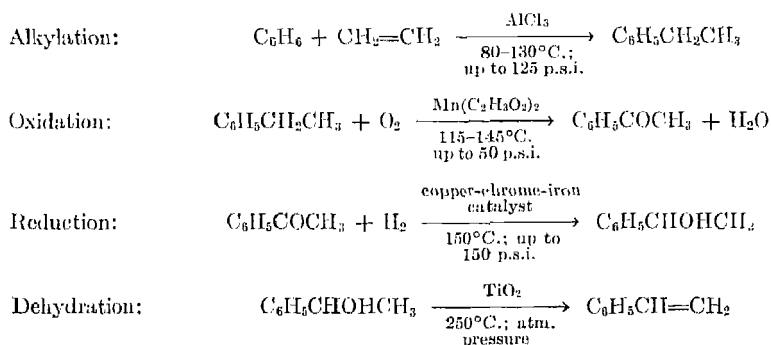
nature of the impurities, a batch of styrene analyzing 99.0% might be preferred to one analyzing 99.95%.

**Foster Grant Process.** A small styrene plant was brought on stream in 1954 by Foster Grant at Baton Rouge (6a). This plant, which is designed to produce only 2,000,000 lb. per month of styrene, is about one-third the size of the smallest of the government plants. Its investment cost is given as \$4,000,000 equivalent to \$333 per annual ton. The process used incorporates some of the early German patents with new design features and in general resembles the German much more closely than it does the Dow process. It is not licensed under American patents. It uses a promoted iron catalyst (Shell 105), which is said to have approximately the following composition:  $\text{Fe}_2\text{O}_3$ , 83%;  $\text{Cr}_2\text{O}_3$ , 2-2.5%; KOH, 12%; NaOH, 1%. It is assumed that the catalyst is in tubes rather than in a massive bed. Like the German process, it uses hydroquinone rather than sulfur and 4-*tert*-butylpyrocatechol (T.B.C.) in the fractionation step.

#### ACETOPHENONE PROCESS

This, like the dehydrogenation processes described above, starts with the alkylation of benzene to form ethylbenzene. The subsequent steps are radically different, involving the oxidation of the ethylbenzene to acetophenone, the partial reduction of the latter to  $\alpha$ -phenylethyl alcohol ( $\alpha$ -methylbenzyl alcohol, phenylmethylecarbinol), and the dehydration of this to styrene.

The four steps may be represented by the following equations (11):



The dehydrogenation and the acetophenone processes for converting ethylbenzene to styrene are excellent examples of the modern physical chemistry approach to a problem as contrasted to the more classical organic chemistry approach. A comparison of the processes also illustrates two important considerations in the selection of one from two or more possible routes for arriving at the same chemical end point. One of these is the ease or difficulty of carrying out on a commercial scale the necessary intermediate unit processes; the other is the possible value of by-products.

Basically, the conversion of ethylbenzene to styrene involves only the relatively simple removal of a molecule of hydrogen, which can be done by a simple heat treatment. Dehydrogenation (with or without a catalyst) is obviously the simplest method of doing this. Practically the major stumbling block is the difficulty of the separation of the styrene from the unconverted ethylbenzene (21). The Dow company and the Koppers and Monsanto companies faced and solved this problem as described above. The Carbide and Carbon Chemicals Company, faced with the same problem, elected

to get around it by adopting a more complicated chemical process than dehydrogenation. One of the advantages is that there is no unusually difficult fractionation step.

A second advantage is that any desired portion of the two intermediate products, acetophenone and  $\alpha$ -phenylethyl alcohol, can be removed, refined, and marketed as such. At present, the commercial demand for the latter is small, but the demand for acetophenone is growing rapidly, having increased in the ten years from 1941 to 1951 from 27,500 lb. to an estimated 350,000 lb. (11). The selling prices of the refined and perfumery grades of acetophenone are about \$0.75 and \$1.30 per pound, respectively, compared to about 21 cents for refined styrene. We thus have the curious situation of an intermediate product being worth several times as much as the final product, because of the effect of the size of the demand on refining costs. It should be noted, however, that the large volume in which styrene is produced permits the production of the crude acetophenone at a lower cost than would be possible if the size of the unit were geared to the current market for that compound alone.

The various steps of the process are not as simple as indicated by the equations since side reactions occur. In the oxidation of the ethylbenzene to acetophenone, for example,  $\alpha$ -phenylethyl alcohol and small quantities of benzoic acid and other products are formed.

**Oxidation.** This is carried out in the liquid phase at a pressure of 30 p.s.i. and at a temperature of 126°C. in two reactors in series, using air as the source of oxygen. The time of contact in each is about 15 hours. The catalyst, manganese acetate, is added continuously as a 15% aqueous solution. The use of two reactors in series permits a faster reaction than would be possible in a single unit of twice the size since the concentration of oxidation products in the first reactor is low. The units are of steel, with an acid-resistant brick lining. The reaction is exothermic, the temperature being controlled by river water through coils of type 304 stainless steel. Other metal parts are of type 347 stainless. About 16% of the ethylbenzene is oxidized in the first reactor. In the second reactor, less air is used and conversion is maintained at about 10% to keep down the formation of by-products. At the conversion level of 26%, the product from the second reactor contains about 17% acetophenone, 8%  $\alpha$ -phenylethyl alcohol, 2% residues and mixed acids, and 73% unreacted ethylbenzene. The ultimate yield is 88–90%.

The product is washed with caustic but is kept on the acid side to prevent the formation of acetophenone condensation products that would form under alkaline conditions in the distillation step. The washed oil is fed to an ethylbenzene stripping still, in which the unreacted ethylbenzene is removed. The column operates at a pressure of 85 mm. with a bottoms temperature of about 145°C. A small bleed stream of nitrogen is introduced to maintain an inert atmosphere.

A mixture of acetophenone and  $\alpha$ -phenylethyl alcohol is separated from the high-boiling residue in a second vacuum still. The overhead mixture does not require separation, since the next step is the hydrogenation of the acetophenone to the alcohol. This is fortunate because the two compounds differ in boiling point by only about 2°C. at atmospheric pressure and 10°C. at 10 mm. When acetophenone is being recovered as such, the separation problem is simplified by sending the mixture to a separate unit in which a considerable fraction of the  $\alpha$ -phenylethyl alcohol is dehydrogenated to acetophenone, together with some styrene, before fractionation.

**Reduction.** The overhead mixture (about 68% acetophenone and 32%  $\alpha$ -phenylethyl alcohol) is hydrogenated in the liquid phase at a moderate temperature

and pressure (about 150°C. and 150 p.s.i.), using a copper-chromium iron catalyst. In this step, some of the alcohol is reduced to ethylbenzene. This must be removed cleanly by vacuum fractionation, otherwise it would appear in the final product. The ethylbenzene, of course, is returned as feed to the oxidation step.

**Dehydration.** The residue after stripping off the ethylbenzene, consisting of the alcohol and some unconverted acetophenone, is then dehydrated in the vapor phase by passing it over titania or other oxide at 200–250°C. The product styrene is separated by fractionation, the unconverted alcohol and acetophenone being taken overhead from the residue and recycled to the hydrogenation step.

It is said that the maximum number of plates required in any step is 34, compared to the 70 used in separating styrene from ethylbenzene, and that the conversions and ultimate yields of the three steps following the alkylation reaction are (4):

Step	Conversion per pass	Ultimate yield
Oxidation	25–26	88–90
Hydrogenation	80	98
Dehydration	80	91

The yield figures correspond to an overall yield of styrene from ethylbenzene of 78–80% compared to 90% by direct dehydrogenation.

Looked at from the point of view of styrene production only, the much more complicated acetophenone process could not compete with the simpler and higher yielding dehydrogenation process, once the major hurdle of separating the styrene from the latter process from ethylbenzene had been solved on a commercial scale. The acetophenone process was closed down for a period of about three years after World War II. However, it is not necessary to look upon this process solely from the point of view of styrene production, and it is now (1954) again in commercial operation. Since the current prices of refined grades of the principal intermediates are much higher than the price of styrene, operation on the large scale of the styrene process permits producing them in crude form at a lower cost than would otherwise be possible, and the profit from them improves the economics of the combined operations. This will still be true if the demand for acetophenone expands to a point large enough to bring the separation and refining costs down to a point that will permit its sale at a price in the same range as styrene.

#### PYROLYSIS OF PETROLEUM

As mentioned above, styrene can be produced by straight thermal cracking of ethylbenzene. It can also be produced by the pyrolysis of petroleum. During World War II, a small commercial unit using the Ugite process was operated using selected crude oil as the charge stock under conditions favoring the formation of aromatics and unsaturates (6). A light oil fraction from this process boiling from about 135 to 150°C. contained ethylbenzene, the xylenes, and styrene. Efficient fractionation concentrated the styrene to approximately 60%, at which point the diluent was essentially *o*-xylene. The essential step in the concentration of the product from this or any other process starting directly with petroleum is thus the separation of styrene, b.p. 145.2°C., from *o*-xylene, b.p. 144.4°C. From the difficulty in separating ethylbenzene from styrene with a spread of 9°C. in the boiling points, it is obvious that sepa-



ration by straight fractionation of *o*-xylene from styrene with a spread of only 0.8°C. is not commercially practicable.

With recent advances in the art of solvent and azeotropic fractionation, this process for the production of styrene may well be reviewed since it is inherently cheap and uses no benzene or other critical raw material. A somewhat similar process known as the Catarole process is in commercial operation in England.

#### STYRENE FROM BY-PRODUCTS

Styrene is present in the light oils, drip oils and, other condensates from the carbonization of coal and from the manufacture of carburetted water gas and oil gas. During World War II, one commercial process produced pure styrene by the thermal depolymerization of low-molecular-weight polymers from by-product styrene. The cost of this process is at present prohibitive, but crude by-product styrene continues to be used for purposes for which the impurities and diluents are not the controlling factors.

#### Economic Aspects

Table VI, compiled from data by the Chemical Division of the U.S. Tariff Commission, shows styrene production from 1940 through 1953. Through 1947, the preponderant part of the styrene produced was consumed in making synthetic rubber, but nonrubber uses (synthetic resins) developed since the war have increased considerably (figures below in millions of pounds):

Year	Produced for synthetic rubber	Produced for synthetic resins	Total production
1950	175	350	539
1951	250	325	708
1952	326	350	700
1953	318	395	799

The current (1954) price is \$0.21 per pound.

Styrene production is intimately interrelated with the coal tar and petroleum industries, because of its large consumption of raw materials from these sources. Styrene production represents the greatest single use of benzene and the third greatest use of ethylene. In 1950, benzene required for styrene production amounted to 65 million gallons, exceeding the total benzene used for phenol and nylon production. This requirement represented such a large percentage of the total benzene available from both by-product coking and from petroleum that it has had a significant effect in stimulating the installation of facilities for producing petrochemical benzene. The ethylene requirement for styrene in 1950 was 173 million pounds, over 10% of the total ethylene production, and exceeded only by the ethylene required for ethyl alcohol and ethylene oxide production. In addition, aluminum chloride requirements in the alkylation stage are significant to the chemical industry.

Styrene production facilities in the U.S. are located in Pennsylvania (Koppers Kobuta plant), West Virginia (Carbide plant at Institute), Michigan (Dow Midland plant), California (Dow Los Angeles plant), Texas (Dow Velasco plant and Monsanto Texas City plant), and Louisiana (Foster Grant Baton Rouge plant).

No figures on the cost of producing styrene have been published by a company

TABLE VI. Styrene Production, 1940-1953.

Year	Quantity, 1,000 lb.
1940.....	2,409
1942.....	9,675
1943.....	97,655
1944.....	349,367
1946.....	405,655
1948.....	376,862
1950.....	539,379
1952.....	699,660
1953.....	799,150
1955 <sup>a</sup> .....	1,000,000
1975 <sup>a</sup> .....	nearly 4,000,000

<sup>a</sup> Estimated by the President's Materials Policy Commission, 1952.

engaged in its manufacture. The best available estimates were published in 1950 by Bohmfalk (2) in connection with the perennial problem of the disposal of the government synthetic rubber plants.

For the three government-built styrene plants at Texas City, Texas, Kobuta, Pennsylvania, and Velasco, Texas, which were sold to private companies in 1946 and 1947, figures have been published for the design capacity, original (1943) investment, estimated depreciated replacement values, and selling prices. Also, except for the selling price, similar data have been published for the unsold Los Angeles plant. Bohmfalk included figures for the demonstrated capacities. These plus the original investment costs permit calculating the latter in terms of demonstrated capacities. For the three plants sold, the (weighted) average is \$269 per ton. The average becomes \$282 if the Los Angeles plant is included. The original investment in the four plants was approximately \$62,000,000.

For these very large plants with capacities of 37,500-96,000 tons per year, an investment of \$250 per ton was taken as typical for 1943 government costs. This was written down to \$155 per ton to represent a government selling price. Working capital was taken as \$17 per ton. Costs were estimated for a plant operating at 50, 70, and 100% of capacity. Overall yields of 85% of theoretical on both ethylene and benzene were assumed.

The (1950) cost of ethylene was taken at 6.5 cents per pound as a realistic figure for a plant operating at near capacity. The delivered cost of benzene was taken as

#### Estimated Styrene Production Cost (1950)

	Cost, ¢/lb.
Ethylene, 0.32 lb./lb. styrene at 6.5 ¢/lb.....	2.08
Benzene, 0.87 lb./lb. styrene at 25 ¢/gal.....	2.96
Processing, chemicals, utilities, other costs.....	2.00
<i>Total operating costs</i> .....	7.04
Depreciation 7.5% of investment.....	0.83
Administration and miscellaneous 2% of sales price.....	0.23
Royalty 5% of sales price.....	0.60
Freight.....	0.23
<i>Subtotal</i> .....	8.93
Return 25% of total capital investment before income tax.....	3.07
<i>TOTAL</i> .....	12.00

25 cents per gallon, the then delivered (Texas) price. No selling expense was allowed because of the assumption of a contract.

The estimate on the preceding page was arrived at for the calculated styrene cost at 70% of demonstrated capacity with a \$155 investment per annual ton of capacity and a \$17 working capital per annual ton of capacity.

For a plant operating at 50 and 100% of capacity, the 12.0 cents would become approximately 14.0 and 10.3 cents, respectively.

The Reconstruction Finance Corporation reported that the cost in the Government Dow-operated Los Angeles plants was 8.76, 9.23, and 8.68 cents per pound for the years 1951-3 respectively (6a).

### Specifications and Analysis (22)

Table VII gives the specifications of one large American producer.

TABLE VII. Specifications for Styrene.

Purity, wt. %, min. ....	99.3
Color, Saybolt, not darker than, max. ....	25
Appearance. ....	Clear
Aldehydes, wt. % as benzaldehyde, max. ....	0.02
Peroxides, wt. % as H <sub>2</sub> O <sub>2</sub> , max. ....	0.01
Sulfur, wt. % total sulfur, max. ....	0.02
Sulfur, wt. % free sulfur, max. ....	0.002
Chlorine, wt. %, max. ....	0.005
Phenylacetylene (ethynylbenzene), wt. %, max. ....	0.015
Polymer, wt. %, max. ....	0.2
Polymer, solubility in benzene. ....	Complete
Viscosity, cps., at 25°C., max. ....	0.80
Inhibitor, 4- <i>tert</i> -butylpyrocatechol, p.p.m. ....	10-15

Commercial shipments show a higher assay than the 99.3% specified; typically, styrene monomer analyses 99.5-99.7%. As stated above as long as the assay is 99% or better, the amounts of some of the specially deleterious impurities are much more important than the exact styrene content.

By far the most widely used technique for styrene content determination is the freezing-point method. Various volumetric titrations of the double bond may be used, although such methods are less accurate and precise than the freezing point. 4-*tert*-Butylpyrocatechol, the standard inhibitor used to prevent premature polymerization of the monomer, may be determined colorimetrically after treatment of the sample with aqueous caustic. Dissolved water may be determined by the Karl Fischer method or a cloud-point technique. Phenylacetylene may be determined by precipitation as the silver acetylide with ammoniacal silver nitrate, followed by solution of the precipitate and volumetric determination of silver with standard thiocyanate. Polystyrene present in the monomer may be determined either by precipitation with a nonsolvent or by distillation. Aldehydes, which form readily in styrene on exposure to air, may be determined by titration of hydrogen chloride liberated on reaction with hydroxylamine hydrochloride.

Peroxides in styrene may be determined by an oxidation-reduction technique based on the oxidation of ferrous to ferric iron and determination of the latter with

standard titanous chloride. Procedures are available for the determination of divinylbenzene, chlorides, sulfur, etc. (4).

### Health and Safety Factors (16)

Styrene is both toxic and flammable, although in both respects it is a less dangerous industrial chemical than benzene and may be safely handled with suitable precautions. The liquid can cause skin irritation on frequent or extended exposure, and the latter should be avoided. The vapor is an irritant to the eyes and respiratory tract; it is readily detectable by its characteristic odor. It has been recommended that vapor concentrations not exceed 400 p.p.m. for an 8-hour exposure. A concentration of 1,300 p.p.m. results in extreme eye and nose irritation; experiments with animals have shown 2,400 p.p.m. for 8 hours or 10,000 p.p.m. for 30-60 minutes may be acutely dangerous, as a result of lung irritation or depression of the central nervous system. Provision of normally adequate ventilation and available standard safety equipment such as showers, eye baths, and goggles should prove satisfactory. Styrene does not show the detrimental hematological effects of benzene.

Due precautions against fire hazard should be observed, although styrene is not sufficiently flammable to be classed as a "Flammable Liquid" by I.C.C. regulations. Styrene vapors should not be exposed to or permitted near open flames, hot spots, static electricity, electrical discharges, or other means of ignition. Ordinary fire extinguishing equipment is effective and should be available.

Styrene is extremely reactive and, in particular, polymerizes readily. The polymerization is exothermic and thermally autocatalytic, and can develop into a runaway reaction of an explosive nature. In shipment and storage an inhibitor, such as 4-*tert*-butylpyrocatechol, is normally added to minimize polymerization. The inhibitor content should be periodically checked. Exposure to elevated temperatures should be avoided. Exposure to air or oxygen should be minimized because styrene tends to react to form aldehydes, peroxides, and polymer, the effect being greater the higher the temperature. The inhibitor present may also be destroyed by excessive air exposure.

Vessels used for storage and shipment of styrene should be clean and constructed of copper-free materials, such as black iron, galvanized iron, steel, and glass. Copper or its alloys, such as brass, bronze, and Monel metal, tend to discolor styrene by forming soluble copper compounds. Obviously undesirable soluble impurities include fats, oils, and waxes. Acids and metal halides react with styrene. Small amounts of residual styrene should be removed before re-use of containers, since undesirable oxidation products may be present.

The Manufacturing Chemists' Association has recommended that shipments of styrene monomer be made in pint or quart glass bottles, one- and five-gallon metal cans, up to 55-gallon drums, in tank trucks, or in tank cars. The same organization has issued recommendations for handling techniques.

### Uses

The preponderant use of styrene monomer is in a variety of polymerization and copolymerization reactions, carried out by emulsion, mass, and solution production methods. Synthetic rubber still accounts for about 40% of the production, but consumption in the resin field has increased greatly in recent years.

It is no longer a simple matter to distinguish between rubber and nonrubber uses,

since emulsion copolymers of styrene and butadiene are now used for many uses far removed from tires. One such rapidly expanding use is in the form of latexes in water-based paints. Polystyrene molding resins were formerly substantially pure styrene polymers, but currently a diversity of polystyrenes is offered by American producers. These resins represent modifications made to improve such properties as impact strength, solvent resistance, or heat distortion. The properties of styrene-butadiene copolymers may be varied over a wide range by varying the ratio of styrene to butadiene, and the high styrene-butadiene copolymers are used in a wide variety of fields from traffic paints and plaster sealers to replacements for leather (particularly shoe soles).

Among other important products are styrenated drying oils, styrenated polyester resins (based largely on maleic anhydride), and styrene-divinylbenzene copolymers from which ion-exchange resins are derived by sulfonation.

To date no significant commercial uses of styrene based on chemical reactions other than polymerization and copolymerization have been developed. The great reactivity, availability, and low price of the monomer may, however, stimulate such development, although it seems most unlikely that the use of styrene as an intermediate will ever approach the use of polymeric reactions.

### Styrene Homologs and Derivatives

Of the various styrene homologs only the methylstyrenes are of current commercial significance. The ring methylstyrenes (vinyltoluenes) are rather similar to styrene in a number of respects, notably in their ready thermal polymerizability.  $\alpha$ -Methylstyrene, in contrast, while readily polymerizable with ionic catalysts, is relatively recalcitrant to free-radical polymerization. Mono- and dichlorinated styrenes have also attracted attention.

**Vinyltoluene**,  $\text{CH}_3\text{C}_6\text{H}_4\text{CH}:\text{CH}_2$ , formula weight 118.17, can be produced from ethylene and toluene in a manner very similar to the production of styrene from ethylene and benzene, although certain additional processing complexities are introduced because of the three possible positional isomers of ethyltoluene and vinyltoluene and the peculiarities of the ortho isomer (4).

Commercial vinyltoluene is a substantially ortho-free mixture of *m*- and *p*-vinyltoluene. It is in many uses a replacement for styrene and, in some uses, may be superior to styrene, as in certain types of coatings. Commercial interest in vinyltoluene has been considerably stimulated by the continuing shortage and high price of benzene and the large quantities of toluene actually or potentially available from petroleum.

The properties of a typical commercial vinyltoluene mixture (65:35 *m*- to *p*-vinyltoluenes) are given in Table VIII.

Vinyltoluene is produced by the vapor-phase dehydrogenation, in the presence of steam, of ethyltoluene, which is produced in turn by the liquid-phase aluminum chloride-catalyzed ethylation of toluene in the presence of a promoter. The ethylation is quite similar to that of benzene and, in fact, proceeds somewhat more readily in the case of toluene. Both direct ethylation and ethyl group interchange reactions proceed in the alkylator. Unreacted toluene and polyethyltoluenes are recycled to the reactor or to a separate reactor in which they are reacted with toluene in the presence of aluminum chloride. The alkylation is complicated by the formation of three positional isomers and by side reactions involving some demethylation of the toluene group giving as by-products benzene, xylenes, and ethylbenzene.

TABLE VIII. Properties of a Commercial Vinyltoluene Mixture.

B.p.	171.45°C.
M.p.	-82.5°C.
$n_D^{20}$	1.5419 (calc.)
Density at 20°C.	0.8970 g./ml.
Refractivity intercept, $n - (d/2)$ , at 20°C.	1.0934
Sp.heat (liquid) at 30°C.	0.450 cal./g.
Viscosity at 25°C.	0.770 cps.
Surface tension at 25°C.	31.0 dynes/cm.
Latent heat of vaporization at 25°C.	116,600 cal./mole
Flash point (Cleveland open cup).	61°C.
Fire point (Cleveland open cup).	60°C.

Before dehydrogenation, it is necessary to remove the *o*-ethyltoluene, for it dehydrogenates in part to indene, which is detrimental to certain properties of the polymers and also undergoes considerably more side reactions in the dehydrogenation. In consequence, the fractionation train required to work up the crude alkylator product is more complex than for ethylbenzene. In addition to the separation of toluene (for recycle), ethyltoluene, and polyethyltoluenes, benzene, ethylbenzenes, and xylenes, and, most difficult of all, *o*-ethyltoluene (b.p. 165.1°C.) must be separated from the mixture of *m*- (b.p. 161.3°C.) and *p*-ethyltoluene (b.p. 162.0°C.). Separation of *o*-ethyltoluene requires an extremely efficient column operating at high reflux, and is carried out continuously. The *o*-ethyltoluene may be recycled to the alkylation process, in which it reaches a steady-state quantity.

With the ortho isomer removed, the dehydrogenation of the *m*- and *p*-ethyltoluene proceeds very similarly to that of ethylbenzene, with a tendency toward slightly less efficiency. The difference of 9.2°C. between the boiling points of the vinyltoluene and *p*-ethyltoluene is the same as the spread between the boiling points of styrene and ethylbenzene. However, the fractionation problem is more difficult because the boiling point of vinyltoluene is about 26 deg. C. higher than that of styrene. Thus a lower still-pot pressure must be maintained in order to keep the temperature down to the level at which polymerization inhibitors are effective.

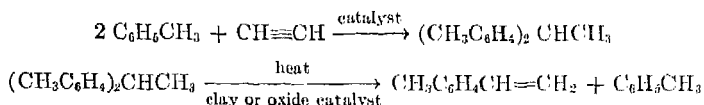
A typical analysis of commercial vinyltoluene is 99.7% unsaturated (mercuric acetate analysis), 0.005% carbonyl groups (as benzaldehyde), 0.0005% chlorine, 0.002% sulfur, 0.004% phenylacetylene, and 0% polymer. Analytical methods are basically similar to those for styrene except that the freezing point method of purity determination is not applicable. Likewise, safety precautions, health hazards, and methods of handling and shipping are fundamentally the same. As in the case of styrene, it is necessary to avoid undesired or premature polymerization, and inhibitors, such as 4-*tert*-butylpyrocatechol can be used for this purpose.

Vinyltoluene, compared to styrene, is only on the threshold of its career industrially. It would be premature to assess the future significance, production, and use patterns, particularly since in part these are dependent on the styrene situation and on benzene-toluene price relations and other factors influencing the relation of styrene-vinyltoluene production costs. Some hints may be gained from the fact that vinyltoluene polymerizes somewhat more rapidly than styrene, has a higher boiling point (advantageous in certain reactions), and offers advantages in preparing styrenated drying oils. In general it may be expected that vinyltoluene will be primarily used in polymerization and copolymerization reactions, as is styrene, that it will in

instances be used as a convenient replacement for styrene, and that new uses and applications will be developed. In the foreseeable future it is unlikely to rival styrene consumption in quantity.

A vinyltoluene plant is under construction by The Dow Chemical Co., a \$10,000,000 Certificate of Necessity having been granted. Volume production is expected in early 1954, and it has been estimated that initial toluene requirements may approximate 700,000 gal. per month.

It is believed that the American Cyanamid Co. may undertake commercial production of vinyltoluene also, the method of manufacture differing sharply from the alkylation-dehydrogenation process developed by Dow (7). The alternative process, on which developmental work has been conducted, involves the acid-catalyzed reaction of acetylene or acetaldehyde with toluene to form asymmetrical ditolyethanes. The latter, on catalytic vapor-phase cracking, yield a mixture comprising primarily toluene and vinyltoluene:



Depending on the conditions used in these steps, the isomer distribution of the final vinyltoluene product can be varied. Of interest is the fact that *o*-vinyltoluene can be satisfactorily produced this way, without the side reactions, including undesirable indene formation, reported in the dehydrogenation of ethyltoluene containing the ortho isomer.

**$\alpha$ -Methylstyrene**,  $\text{C}_6\text{H}_5\text{CH}(\text{CH}_3):\text{CH}_2$ , is isomeric with vinyltoluene but, as a result of the influence of the methyl substituent in the vinyl side chain, differs in several respects from both vinyltoluene and styrene. It has been and is being produced by The Dow Chemical Co. (4) by an alkylation-dehydrogenation process similar to that described for styrene and vinyltoluene, except that benzene and propylene are used as starting materials. It also occurs as a by-product in the manufacture of phenol and acetone from cumene hydroperoxide (10) (see Vol. 10, p. 293), and its recovery and sale affect the economics of this process.

The properties of  $\alpha$ -methylstyrene are given in Table IX.

TABLE IX. Properties of  $\alpha$ -Methylstyrene.

Property	Value
B.p. ....	165.38°C.
F.p. ....	-23.21°C.
$n_D^{20}$ .....	1.5386
$d_4^{20}$ .....	0.9106
Refractivity intercept, $n - (d/2)$ , at 20°C. ....	1.0833
Sp.heat. ....	0.489 cal./g./°C.
Viscosity at 20°C. ....	0.940 cps.
Surface tension at 25°C. ....	32.8 dynes/cm.
Latent heat of vaporization. ....	96,660 cal./mole
Flash point (Cleveland open cup). ....	58°C
Fire point (Cleveland open cup). ....	58°C

The propylation of benzene to form cumene is readily effected by aluminum chloride in the liquid phase, using apparatus and technique similar to that for ethylating

benzene. Propylene is more reactive than ethylene, and the reaction proceeds even more readily. It may be noted that large quantities of cumene for aviation fuel were produced in the World War II largely by the vapor-phase, solid phosphoric acid-catalyzed reaction of propylene and benzene, although some was also produced in a liquid-phase process using sulfuric acid as a catalyst.

The vapor-phase dehydrogenation of cumene to  $\alpha$ -methylstyrene is effected catalytically in the presence of steam in essentially the same manner as is that of ethylbenzene to styrene. The dehydrogenation of cumene proceeds more readily than that of ethylbenzene. Some complications are present in the recovery of high-purity (typically 99.5%)  $\alpha$ -methylstyrene by fractionation of the crude dehydrogenate. Some benzene, toluene, ethylbenzene, and styrene are formed in addition to the desired  $\alpha$ -methylstyrene, and the fractionation train is designed for the appropriate separations.

If the production of phenol from cumene via cumene hydroperoxide increases, it may be expected that additional quantities of by-product  $\alpha$ -methylstyrene will become commercially available.

$\alpha$ -Methylstyrene is relatively unreactive as regards thermal or free-radical polymerization. It readily polymerizes with Friedel-Crafts catalysts, including aluminum chloride and sulfuric acid, and this reaction has been rather extensively studied, particularly at low temperatures. Low polymers of  $\alpha$ -methylstyrene have been produced for use as plasticizers. Also,  $\alpha$ -methylstyrene may be copolymerized with styrene and drying oils, in the production of styrenated drying oils. The  $\alpha$ -methylstyrene is advantageous in moderating the reaction and, as a result, in aiding in the production of compatible products.

**The methyl- $\alpha$ -methylstyrenes.** Of these, the best known is the para isomer. Kobe and Romans (14) obtained it in good yields at high conversions using a chromium oxide catalyst in the dehydrogenation of *p*-cymene (*p*-isopropyltoluene). The latter is obtained as spruce turpentine in the sulfite pulping of eastern spruce. A mixture of the isomeric isopropyltoluenes can be produced readily by the alkylation of toluene with propylene by processes analogous to those used in the production of ethylbenzene or isopropylbenzene. The mixture can be dehydrogenated to a mixture of the methyl- $\alpha$ -methylstyrenes.

The methyl- $\alpha$ -methylstyrenes resemble  $\alpha$ -methylstyrene in their resistance to thermal polymerization, and in their ready polymerization by other methods. Powers reported on a series of copolymers of the para isomer and butadiene (17). He found that they were superior to the styrene copolymers in tensile strength and that they more nearly resemble natural rubber in processing characteristics.

*p*, $\alpha$ -Dimethylstyrene has been produced in relatively small quantities by passing terpenes over a heated oxide catalyst, but this process gave relatively low yields. As of 1954, none of the methyl- $\alpha$ -methylstyrenes is being produced on a commercial scale.

**Dimethylstyrene (vinylxylene),**  $(\text{CH}_3)_2\text{C}_6\text{H}_3\text{CH}:\text{CH}_2$ . By the use of xylene (*m*-xylene is particularly reactive) in the reaction with acetylene or acetaldehyde described on p. 143, vinylxylenes may be prepared. Their polymers have desirable heat-distortion temperatures.

**Halogenated Styrenes.** Of the halogenated styrene resins, the substituted mono- and dichlorostyrenes have aroused the most interest because of the effect of the chlorine atom in increasing the polymerization rate and in raising the heat distortion tem-



perature, improving the chemical resistance, and providing some degree of flame resistance in their polymers.

One of several methods of producing *chlorostyrene*,  $C_6H_4ClCH=CH_2$ , is the catalytic dehydrogenation of each isomer of monochlorinated ethylbenzene. The precautions to be followed to prevent polymerization of the resulting monomers are the same as with styrene. The individual isomers and mixtures of them readily polymerize, giving polymers having the properties previously noted. Chlorostyrenes will also readily copolymerize with such materials as butadiene, styrene, and methyl methacrylate, giving polymers useful in producing improved synthetic rubber with high tensile strength and tear resistance, improved heat distortion characteristics, and some degree of fireproofness.

Substitution of a second chlorine atom yields *dichlorostyrene*,  $C_6H_3Cl_2CH=CH_2$ , (mixture of isomers) a monomer which readily polymerizes and copolymerizes to give polymers of improved heat and fire resistance. The literature describes several methods for its preparation. One process describes its preparation from dichlorobenzaldehyde. Carbinols are formed through Grignard reaction and subsequently dehydrated in the vapor phase over activated alumina. Dichlorostyrene is polymerized very rapidly by thermal, emulsion, suspension, and low-temperature methods.

The polymers produced from isomers of dichlorostyrene are characterized by being self-extinguishing, by having heat distortion temperature of 230 to 250°F., by their higher densities, and by the necessity for higher molding temperatures for fabrication.

Dichlorostyrene isomers copolymerize readily with many monomers, among them styrene,  $\alpha$  methylstyrene, butadiene, and methyl methacrylate. The outstanding uses for these copolymers have been in the development of improved heat resistance copolymers with styrene suitable for molding, and a GR-S rubber with improved heat resistance, tensile strength, aging and resistance to flex cracking.

### Bibliography

- (1) Aston, H. W., and Flavel, T. W., B.I.O.S. Trip 3057 Technical Information and Documents Unit; 40 Cadogan Sq.; London, England.
- (2) Bohmfalk, J. F., Jr., *Chem. Eng. News*, **28**, 2504 (1950).
- (3) Bond, C. R., Jr., *Ind. Eng. Chem., Anal. Ed.*, **19**, 390 (1947).
- (4) Boundy, R. H., and Boyer, R. F., *Styrene* (A.C.S. Monograph No. 115), Reinhold, N.Y., 1952.
- (5) Bywater, S., *J. Polymer Sci.*, **9**, 417 (1952).
- (6) Chaney, N. K., Hall, E. L., Skeen, J. R., and Smoker, E. H., *Chem. Eng. Progress*, **45**, 71 (1949).
- (6a) *Chem. Week*, **74**, 28 (1954); *Chem. Eng. News*, **32**, 1870 (1954).
- (7) Dixon, J. K., and Saunders, K. W., *Ind. Eng. Chem.*, **46**, 652 (1954).
- (8) Dolliver, M. A., Gresham, T. L., Kistiakowsky, G. B., and Vaughan, W. E., *J. Am. Chem. Soc.*, **59**, 831 (1937).
- (9) Emerson, W. S., *Chem. Revs.*, **45**, 183 (1949).
- (10) Enos, H. T., Jr., and Nixon, J. R., Jr., *Abstracts of Papers 124th Meeting Am. Chem. Soc. (Chicago)*, September 1953, p. 14Q.
- (11) Keag, H. F., and McCullough, *Ind. Eng. Chem.*, **45**, 2 (1953).
- (12) Kearby, K. K., *Ind. Eng. Chem.*, **42**, 295 (1950).
- (13) Kilpatrick, J. E., Beckett, C. W., Prosen, E. J., Pitzer, K. S., and Rossini, F. D., *J. Research Natl. Bur. Standards*, **42**, 225 (1949).
- (14) Kobe, K. A., and Romans, R. T., *Ind. Eng. Chem.*, **43**, 1755 (1951).
- (15) Mavity, J. M., Zetterholm, E. C., and Hervert, G. I., *Ind. Eng. Chem.*, **38**, 829 (1946).
- (16) Mfg. Chemists Assoc., *Chem. Safety Data Sheet*, **SD-37** (1951).
- (17) Powers, P. O., *Ind. Eng. Chem.*, **38**, 837 (1946).

- (18) Roberts, D. E., Walton, W. W., and Jessup, R. S., *J. Research Natl. Bur. Standards*, **38**, 627 (1947).  
 (19) *Selected Values of Properties of Hydrocarbons* (A.P.I. Research Project 44), Carnegie Press, Pittsburgh, Pa., 1953.  
 (20) Sherwood, P. W., *Petroleum Processing*, **8**, 724 (1953).  
 (21) Stanley, A. M., *Chemistry & Industry*, **1938**, 93.  
 (22) Ward, A. L., and Roberts, W. J., *Styrene*, Interscience, N.Y., 1951.  
 (23) Webb, G. A., and Corson, B. B., *Ind. Eng. Chem.*, **39**, 1153 (1947).  
 (24) Wenner, R. R., and Dybdal, E. C., *Chem. Eng. Progress*, **44**, 275 (1948).  
 (25) U.S. Pat. 2,295,612 (Sept. 15, 1942), F. J. Soddy (to U.G.I. Co.).

A. L. WARD AND W. J. ROBERTS

**STYRENE BROMIDE**,  $C_6H_5CHBrCH_2Br$ . See *Bromine compounds (organic)*, Vol. **2**, p. 656.

**STYRENE OXIDE**,  $O\text{---}\underset{\text{CH}_2}{\text{CH}}\text{---}CHC_6H_5$ . See *Ethylene oxide*, Vol. **5**, p. 923.

## STYRENE RESINS AND PLASTICS

Polymerization and copolymerization. . . . .	p. 146	Styrene-based latexes. . . . .	p. 172
Styrene-based plastics. . . . .	p. 157	Styrene-based resins. . . . .	p. 175

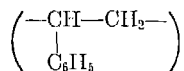
The first commercial process for producing styrene was operated by the Naugatuck Chemical Co. in 1925, but, owing to many difficulties, manufacture was soon discontinued. At about the same time I. G. Farbenindustrie began development work in Germany which was carried through to successful commercial conclusion (6). In 1930 The Dow Chemical Co. entered the styrene field and ultimately became the first company in the U.S. to produce commercial styrene successfully. With the advent of World War II and the resulting loss of natural rubber resources, the combined efforts of Carbide and Carbon Chemical Corp., Koppers Co., Monsanto Chemical Co., and The Dow Chemical Co. supplied up to 200,000,000 lb. of styrene monomer per year to be polymerized with butadiene in the production of GR-S rubber. See also *Rubber, synthetic; Styrene*.

The tremendous expansion of styrene monomer production facilities and the wealth of experience obtained by the above companies laid the groundwork for the postwar development of polystyrene and styrene copolymer plastics. Latexes for paper coatings, styrenated drying oils, and styrenated alkyds as a base for many protective coatings, styrene-polyester resins for laminated structures of exceptional strength, and the production of many materials such as styrene oxide, styrene glycols, and hexene illustrate still further uses for styrene, which has become a chemical basic to many factors of our economy ranging from synthetic rubber automobile tires to high impact polystyrene refrigerator parts and styrene-based latex paints.

## Polymerization and Copolymerization of Styrene

### POLYMERIZATION OF STYRENE

Styrene polymerizes in head-to-tail fashion giving



The polymerization is a chain reaction and proceeds readily with or without catalysts by all known polymerization techniques. Its rate of polymerization increases exponentially with temperature, and formation of water-white polymer of high clarity and excellent physical and electrical properties results. During polymerization, heat is evolved at the rate of 160 cal. per gram, the density changes from 0.905 for pure monomer to 1.045 for pure polymer, the molecular weight increases from 104 for the monomer to 250,000 for commercial molding polymers, and the monomer changes from an aromatic, chemically reactive liquid to an inert, tough, high-molecular-weight, amorphous solid. Figure 1 illustrates the correlation between weight average molecular weight of polystyrene and 10% solution viscosity in toluene.

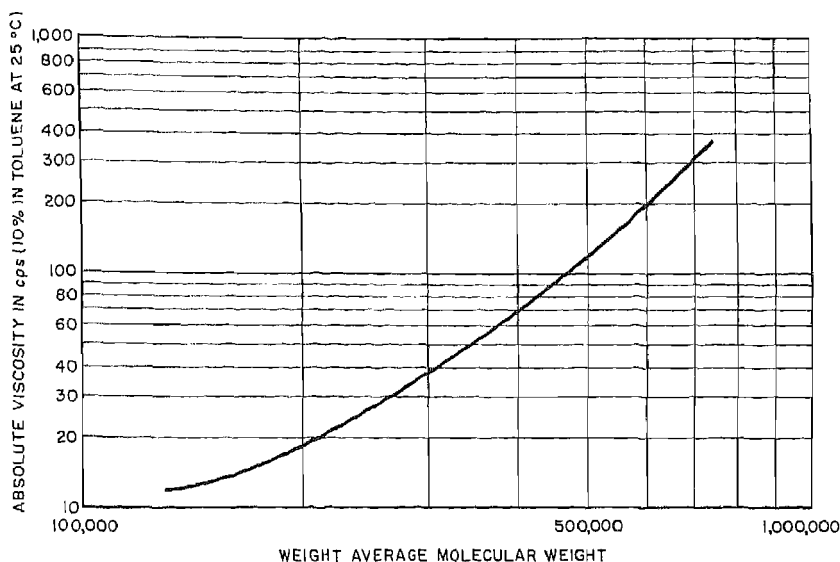


Fig. 1. Weight average molecular weight of polystyrene vs. 10% solution viscosity in toluene.

The process of polymerization of styrene can be resolved into three steps: (1) chain initiation, (2) chain growth, and (3) chain termination. In general, a certain rate constant can be assigned to each of these steps; thus,  $k_i$ ,  $k_p$ , and  $k_t$  signify the constants for initiation, growth, and termination, respectively. Each of these reaction steps obeys an Arrhenius type of equation,  $\text{rate} = Ae^{-E/RT}$ , with different frequency factors ( $A_1$ ,  $A_2$ , etc.) and different activation energies ( $E_1$ ,  $E_2$ , etc.) for each step. Table I compares the rate constants for polymerization of styrene as obtained by various workers, and Table II illustrates values for the frequency factors and activation energies (5).

Chain initiation, growth, and termination proceed as in most polymerization reactions. First, the ethylenic double bond in styrene is opened with the formation of an energy-rich molecule capable of further reaction. Styrene monomer rapidly adds to the free radical at a rate depending exponentially on temperature and much more rapid than for initiation. Four types of chain termination reactions may occur: (1) self-termination; (2) mutual termination, by either combination or disproportionation; (3) chain transfer—transfer of the free radical of a growing chain to another

monomer, solvent molecule, polymer chain, or impurity molecule; and (4) degradative chain transfer where new free radicals do not readily add new monomer units to build chains.

Self-termination, mutual termination, and degradative chain transfer result in destruction or inactivation of activated chain ends which, when sufficient, causes polymerization to cease. The chain transfer termination mechanism describes the transfer of free radical activity from a growing chain to another monomer, solvent molecule, or polymer chain. The newly activated monomer, solvent molecule, or polymer chain now starts a new growing chain while the activity of the original growing chain has ceased. In other words, for each activated radical destroyed a new one is created to start a new chain. A rate constant  $k_t$  describes this process, while  $k_i$  describes the rate constant for actual cessation of the polymerization reaction. Chain

TABLE I. Comparison of Rate Constants for Styrene Polymerization.

Temp., °C.	Polymerization type	Initiation, $k_i$	Propa- gation, $k_p$	Termination, $k_t$	Transfer, $k_f$	Reference
25	Photoinitiation in mass	$1.34 \times 10^{-16}$	39.5	$5.96 \times 10^6$	$1.26 \times 10^{-3}$	(5)
25	Photoinitiation in mass	$1.32 \times 10^{-16}$	18.7	$2.79 \times 10^6$	$0.67 \times 10^{-3}$	(3)
30	Photoinitiation in mass	—	52.0	$10.2 \times 10^6$	$1.66 \times 10^{-3}$	(9)
50	Emulsion	—	39.0	$30 \times 10^6$	—	(15)

TABLE II. Frequency Factors and Activation Energies for Styrene Polymerization.

Factors and energies	Burnett	Bamford and Dewar	Smith	Matheson
$A_i$ (initiation)	$4.15 \times 10^{11}$	$1.23 \times 10^{12}$	—	—
$A_p$ (propagation)	$1.44 \times 10^6$	$1.02 \times 10^6$	$3.5 \times 10^{10}$	$1.2 \times 10^{10}$
$A_t$ (termination)	$1.48 \times 10^8$	$3.07 \times 10^8$	—	$1.2 \times 10^{10}$
$A_f$ (transfer)	$4.08 \times 10^7$	—	—	—
$E_i$ , kg.-cal./mole	36.4	37.0	—	—
$E_p$ , kg.-cal./mole	6.3	6.5	11.7	9.0
$E_t$ , kg.-cal./mole	1.9	2.8	—	3.0
$E_f$ , kg.-cal./mole	14.4	14.2	—	—

transfer termination mechanism is referred to as degradative chain transfer when the new radicals formed do not readily add new monomers to chains and thus cause the reaction to terminate.

The chain transfer termination mechanism is the most probable. Figure 2 illustrates the initial uncatalyzed rate of styrene polymerization at increasing temperatures and the effect of polymerization temperatures on the molecular weight of polystyrene. (The fact that one curve was determined on a highly purified sample of styrene and the other on commercial monomer is not significant.)

It is well known that as polymerization approaches 90% completion, the rate at which the remaining monomer reacts decreases rapidly. The quality of commercial polystyrene is adversely affected by excess unreacted styrene monomer; thus it is important to approach 100% polymerization as closely as possible. Figure 3 illustrates the progress of polymerization at various temperatures, and Figure 4 illustrates

the reduction in volatile content of polystyrene as complete polymerization is approached. These figures show that it may be commercially impractical to carry out such long polymerization schedules to reduce the volatile content to the desired level.

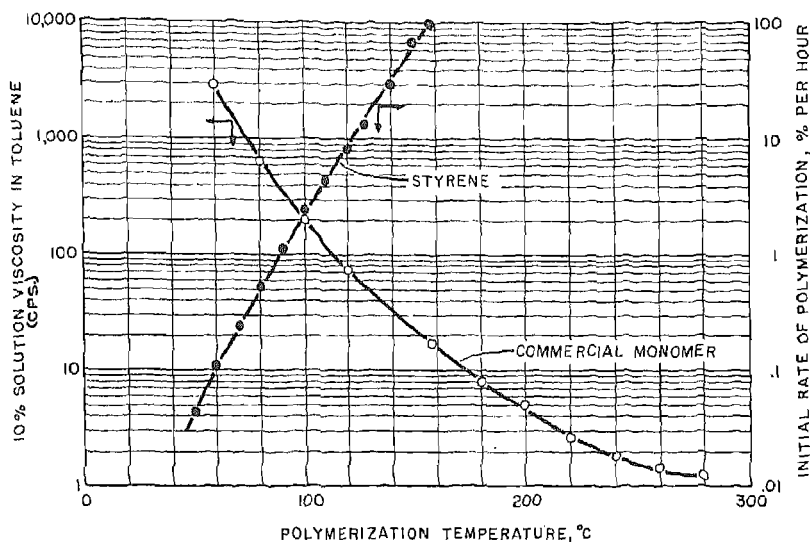


Fig. 2. Effect of temperature on initial rate of polymerization and molecular weight of polystyrene. (Molecular weight in terms of 10% solution viscosity of polystyrene in toluene.)

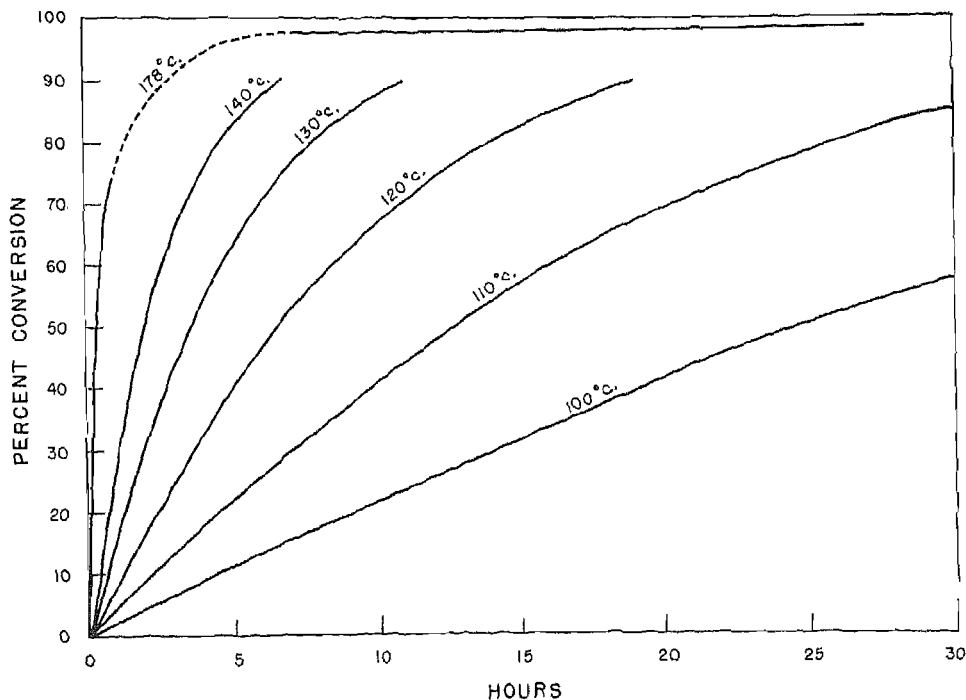


Fig. 3. Effect of polymerization temperature on rate of styrene polymerization (4, p. 218).

Brief finishing treatments at high temperature, special catalysts used at moderate temperatures, and steam and vacuum devolatilization of the finished product are methods used commercially to solve this problem. The presence of volatile materials in polystyrene lowers the heat distortion temperature linearly and may cause crazing if the amount is greater than about 3%. Crazing leads to premature mechanical failure of the molded article. Polystyrene completely free of volatile materials will have a heat distortion temperature in the range of 90–100°C. Commercial polystyrene usually contains not more than 2% volatile materials of which less than  $\frac{1}{2}\%$  is unreacted styrene monomer.

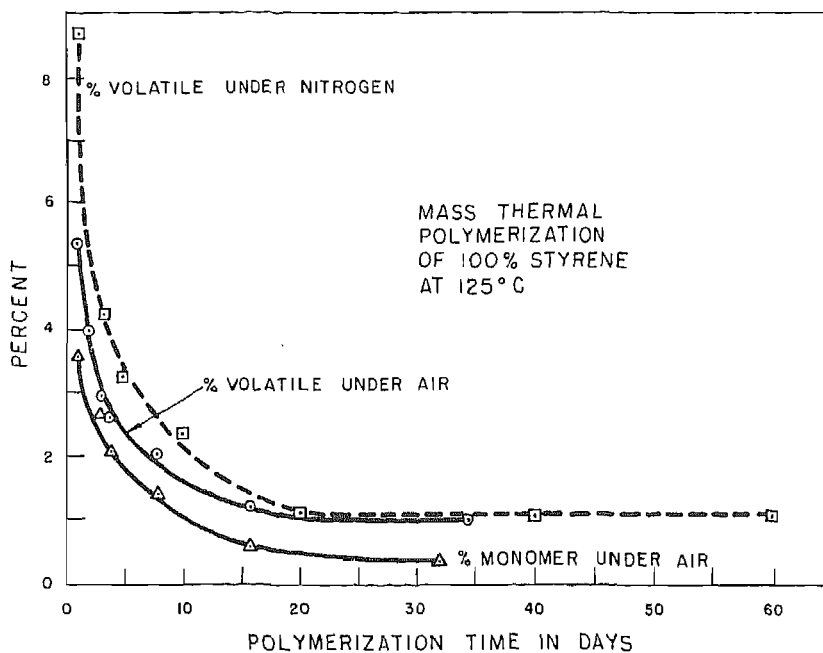


Fig. 4. Effect of polymerization time on volatile content in polystyrene.

**Catalyzed Polymerization of Styrene.** The rate of styrene polymerization can be greatly increased through the use of various catalysts such as, for example, light, organic peroxides, ozonides, and other compounds which readily form free radicals. The use of 0.2% benzoyl peroxide increases the speed of polymerization ten times at 50°C. Figure 5 illustrates the effect of several catalysts on the reaction time at 100°C. Combinations of catalysts with different decomposition rates and temperatures may be used to accomplish rapid polymerization without excessive temperature rise and reduction of molecular weights. Their use can also provide a finishing treatment to reduce the volatile content of the polymer.

An increase in the amount of catalyst or in the temperature increases the rate of reaction and lowers the molecular weight. Since increases in temperature and in catalyst both increase polymerization rates, catalysts can be most advantageously employed at lower polymerization temperatures. As a general rule, the molecular weight of the polymer will vary inversely with the square root of the catalyst concentration.

The peroxide catalysts employed function in a manner typical of free radical catalytic polymerization. Evidence points to the cleavage of benzoyl peroxide into two free phenyl or benzoyl radicals which promote opening the ethylenic double bond in styrene monomer, forming a free radical which can add monomer units to form a polymer chain. This chain reaction continues until the free radical at the end of the growing chain is destroyed by one of the termination mechanisms already discussed. It should be noted that the benzoyl radical may terminate as well as start a growing chain.

**Retarders and Inhibitors.** The compounds which have a negative effect on styrene polymerization fall into two classes, inhibitors and retarders. Inhibitors

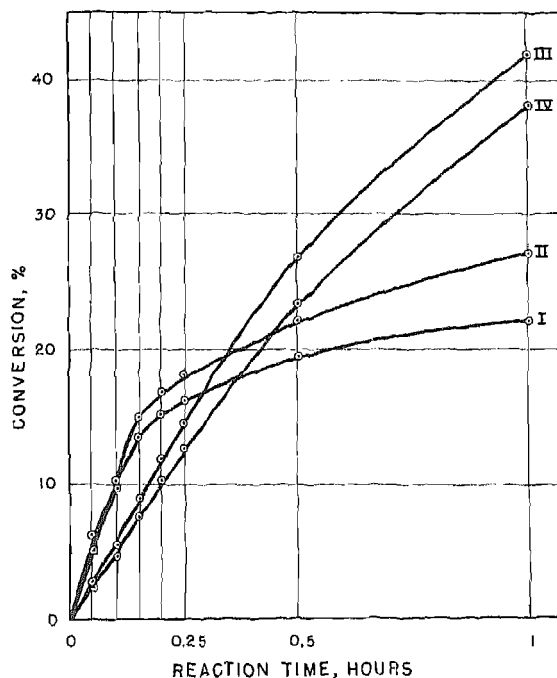


Fig. 5. Per cent conversion of styrene to polystyrene, initial peroxide concentration 0.0133 mole per liter, at 100.0°C. (4, p. 243). I, Bis(2,4-dichlorobenzoyl) peroxide; II, Lauroyl peroxide; III, Benzoyl peroxide; IV, bis(*p*-chlorobenzoyl) peroxide.

extend the induction period probably by destruction of the active centers formed during the initiation process. Retarders reduce the rate of polymerization by interference with the growing chains. Generally, the distinction between inhibitors, retarders, and chain transfer agents can be pictured as a continuous sequence rather than as sharp classifications. Thus a degradative chain transfer agent may be called a retarder or, if active enough, an inhibitor.

Figure 6 illustrates the effect of inhibitor concentration on the induction period at 80°C. It also illustrates one of the reasons for the widespread commercial use of *p*-*tert*-butylpyrocatechol as a storage inhibitor for styrene, namely, its relatively high efficiency at low concentration. If excess amounts are present, they will not appreciably affect the induction period. In addition, it does not seriously interfere with

polymerization at higher temperature and may be removed from the monomer with a caustic wash if desired. The life of a storage inhibitor is a function of the storage temperature. Generally 1-5 p.p.m. of *p*-*tert*-butylcatechol will prevent polymerization of styrene monomers for ample periods of time under most storage and shipping conditions. Excessive contact of styrene monomers with air or catalytic agents which

TABLE III. Polymerization Techniques, Their Advantages, Disadvantages, and Cost Factors.

Method	Polymerizing system	Advantages	Disadvantages	Cost factors
Batch mass polymerization	Pure styrene monomer in individual containers	1. Simplicity 2. Excellent electricals 3. High clarity	1. Heat evolution serious in large-scale operation 2. Broad distribution of molecular weight 3. Containers limited to diameters of 6-10 in.	1. Containers 2. Polymerization baths and handling equipment 3. Grinding
Solution polymerization (Ref. 4, pp. 272-74; Ref. 20)	Styrene monomer diluted with solvent	1. Controlled heat of polymerization 2. Polymer already in solution for lacquers, etc.	1. Difficult to remove last 10% of solvent 2. Solvent reduces molecular weight and rate of polymerization 3. Mechanical problems in stirring highly viscous solutions	1. Polymerization equipment 2. Drying of polymer 3. Solvent recovery 4. Grinding
Emulsion polymerization (Ref. 4, pp. 274-87; Refs. 18, 20, 21, 23)	Water used as carrier with emulsifying agent to give extremely small particles, and catalyst to give fast rate	1. Rapid and no difficulty with heat of polymerization 2. Many copolymerizations not possible by other techniques proceed readily in emulsion 3. Adaptable to continuous polymerization 4. Usefulness of latexes 5. Simple kettles for polymerization 6. Polymer has higher heat distortion temperature (by 10 deg. C.) than mass polymer	1. Contamination of polymer with water and emulsifying agents 2. Molecular weight of polymer high for fast injection molding 3. Color and clarity of polymer deficient	1. Catalysts 2. Emulsifiers and stabilizers 3. Coagulants 4. Washing and drying of polymer 5. Pelletting of dried polymer



TABLE III. Polymerization Techniques, Their Advantages, Disadvantages, and Cost Factors (Concluded).

Method	Polymerizing system	Advantages	Disadvantages	Cost factors
Suspension polymerization (Ref. 4, pp. 274-87; Refs. 20, 22, 24)	Water used as a carrier with stabilizing agents such as starch to keep material in suspension, and one or more catalysts to speed up polymerization	<ol style="list-style-type: none"> <li>1. No difficulty with heat of polymerization</li> <li>2. Simple kettles for polymerization</li> <li>3. Volatile can be reduced to low level by suitable choice of catalysts and temperature schedules</li> </ol>	<ol style="list-style-type: none"> <li>1. Possible contamination from water and stabilizing agent</li> </ol>	<ol style="list-style-type: none"> <li>1. Same as for emulsion polymerization</li> </ol>
Continuous mass polymerization (Refs. 19, 26)	Pure styrene monomer fed continuously to reactor	<ol style="list-style-type: none"> <li>1. More uniform product</li> <li>2. High clarity</li> <li>3. Excellent color</li> </ol>	<ol style="list-style-type: none"> <li>1. Mechanical problem in moving highly viscous finished polymer</li> </ol>	<ol style="list-style-type: none"> <li>1. Expensive equipment</li> <li>2. Slow rate of production per unit volume of equipment</li> </ol>
Ionic polymerization	Styrene and other monomers diluted with solvent such as methylchloride	<ol style="list-style-type: none"> <li>1. Can produce copolymers that cannot be produced readily by other polymerization methods, for example, styrene-isobutylene copolymer</li> <li>2. Low-pressure operation with low-boiling monomers</li> <li>3. Rapid polymerization rate</li> </ol>	<ol style="list-style-type: none"> <li>1. Corrosive catalyst used—<math>\text{AlCl}_3</math></li> <li>2. Difficulty in maintaining good color</li> <li>3. Need of washing, neutralizing, and drying polymers</li> <li>4. Low-temperature refrigeration needed</li> </ol>	<ol style="list-style-type: none"> <li>1. Expensive equipment</li> <li>2. Recovery of solvent and recycle</li> <li>3. Catalyst</li> <li>4. Refrigeration cost</li> </ol>

might be present in the container may greatly reduce the period of safe storage. As a rule of thumb, the inhibitor life decreases threefold with each 10 deg. C. increase in storage temperature.

The presence of solvents such as ethylbenzene, toluene, carbon tetrachloride, and benzene during styrene polymerization depresses the rate of polymerization and the molecular weight of the polymer. These solvents act as chain transfer agents whose action is slightly temperature-dependent, increasing at higher temperatures. Figure 7 illustrates the effect of several polymerization solvents on the molecular weight of polystyrene as indicated by 10% solution viscosity. It should be noted that, as the solvent concentration is increased, the molecular weight is decreased. The preparation of low molecular polystyrenes may be accomplished through addition of solvent as noted above and/or by high polymerization temperatures and large amounts of

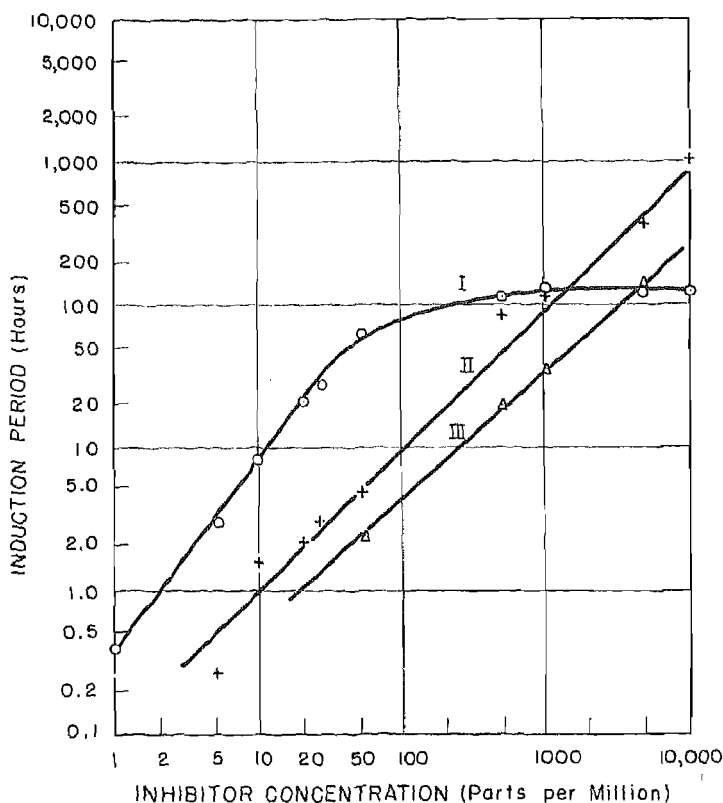


Fig. 6. Effect of several polymerization inhibitors on induction period at 80°C. (4, p. 262). I, *p*-*tert*-butylpyrocatechol; II, 2-nitro-4,6-dichlorophenol; III, sulfur. The induction period is taken as the time required for the sample to reach a relative viscosity of 1.1.

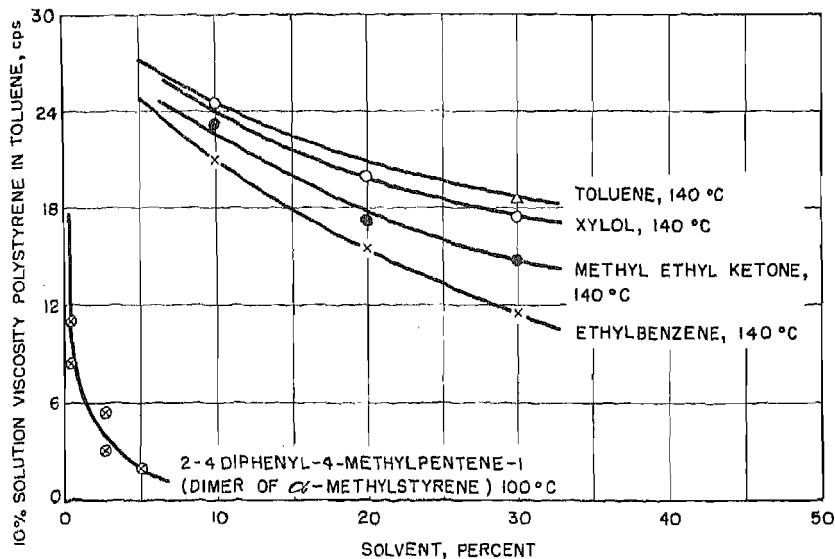


Fig. 7. Effect of several solvents as chain transfer agents in terms of solution viscosity.

catalyst. When large amounts of solvent are used, solvent recovery and drying the polymer may be a problem.

**Comparison of Methods of Polymerization.** The technique of polymerization used will be dictated in part by the scale of operation and the intended use of the polymer (20). A cost comparison of the various techniques is a detailed problem in chemical engineering which can only be answered by a consideration of accurate laboratory and pilot plant data and the intended use of the product. Table III summarizes the various methods of polymerization and some factors affecting the cost of each type.

Table IV summarizes the data of Samaras and Perry (13) on the relative capital cost, conversion cost, and total cost for three common methods of polymerization. The total cost includes raw materials as well as direct and indirect costs. Many assumptions regarding both financial and technical aspects had to be made. They concluded that the difference in total production cost by any of the three methods now in commercial use is small providing each process has been worked out to a high degree of perfection and that production volume is large.

TABLE IV. Relative Costs of Three Polymerization Methods.

Method of polymerization	Relative capital cost	Relative conversion cost	Relative total cost
Mass	1.6	1.15	1.00
Suspension	1.7	1.00	1.10
Emulsion	1.0	1.10	1.05

#### COPOLYMERIZATION OF STYRENE

In general, the methods for polymerization of styrene can be employed for copolymerization of styrene with many other monomers. The same considerations of economics, type of polymer desired, and scale of operation dictate the particular method to be used. Styrene may be polymerized with many monomers, a complete listing of which appears in the literature (4, pp. 960-1057). The most extensive work on styrene copolymers has been with styrene-butadiene systems for synthetic rubber and thermoplastic applications. Copolymers of styrene with polyesters,  $\alpha$ -methylstyrene, and drying oils have been prepared commercially for application in the protective coatings field; with divinylbenzene for the production of ion-exchange resins; and with acrylonitrile, methyl methacrylate,  $\alpha$ -methylstyrene, and divinylbenzene in the plastics field. These are only a few of the more common systems.

Peroxide catalysts are generally employed and serve to control the rate of polymerization at lower temperatures and thus provide a means of controlling the properties of the resultant polymer. The action of the catalyst during the initial stage of a copolymerization is identical with that occurring in polymerization, namely, the formation of a free radical making possible the interaction of the monomer units.

Much can be learned about copolymerization from the propagation or growth reactions. The rate of copolymerization and the molecular weight of the resulting polymer are dependent on the rate of initiation and termination, but the chemical composition and the molecular structure of the copolymer are almost entirely dependent on the competition of the two monomers for both types of free radicals or growing chain ends. Assuming a binary system, Table V illustrates the propagation reactions taking place.  $M_1$  and  $M_2$  are two monomers and  $M_1^*$  and  $M_2^*$  are concen-

trations of active chain ends of  $M_1$  and  $M_2$ . Since the rate of reaction of each growing chain with monomer differs, the initial polymer formed is richer in the more reactive component. As the more active component is consumed, the latter polymer formed is richer in the less reactive component. Thus, the overall product is a mixture of copolymer molecules of different chemical constitutions.

TABLE V. Reaction Combinations in Binary Copolymerization Systems.

Growing chain	Monomers adding	Rate of process	Reaction product
$M_1^*$	$M_1$	$k_{11}(M_1^*)(M_1)$	$-M_1-M_1^*$
	$M_2$	$k_{12}(M_1^*)(M_2)$	$-M_1-M_2^*$
$M_2^*$	$M_1$	$k_{21}(M_2^*)(M_1)$	$-M_2-M_1^*$
	$M_2$	$k_{22}(M_2^*)(M_2)$	$-M_2-M_2^*$

The tendency of any one of the four addition reactions pictured in Table V to predominate over any other is a function of the reactivity of the monomers in question. The reactivity controls the competition of each monomer for each type of free radical. Table VI gives the relative reactivities of several monomers with several radicals. The reactivity of a monomer toward its radical has been arbitrarily set at unity. Values greater than unity indicate higher reactivity of the radical in question with a given monomer than with its parent monomer. Table VII indicates the instantaneous composition of several styrene copolymers with varying amounts of styrene present in the initial monomer mixture. These compositions are taken from copolymer composition curves based on values of reactivity ratios  $\sigma$  and  $\mu$  for the system in question.

$$\sigma = \text{reactivity ratio } k_{gA}(A)/k_{gB}(A)$$

$$\mu = \text{reactivity ratio } k_{gB}(B)/k_{gA}(B)$$

where  $k_{gA}(A)$  = rate constant for propagation by addition of A— monomer to a radical with an active A— end;  $k_{gB}(A)$  = rate constant for propagation by addition of B— monomer to a radical with an active A— end;  $k_{gA}(B)$  = rate constant for propagation by addition of A— monomer to a radical with active B— end;  $k_{gB}(B)$  = rate constant for propagation by addition of B— monomer to a radical with an active B— end. The literature indicates rather wide limits for values of  $\sigma$  and  $\mu$ . For this

TABLE VI. Relative Reactivity of Various Monomers with Various Radicals.

Monomer	Radical							
	Styrene	Methyl methacrylate	Acrylonitrile	Vinylidene chloride	Iso-prene	Buta-diene	Chloro-prene	Vinyl acetate
Styrene	1.0	2.0	25	7	0.5	0.7	0.2	—
Methyl methacrylate	2.0	1.0	7	4.1	—	1.3	—	—
Acrylonitrile	2.5	0.8	1.0	2.7	2.2	3.1	0.2	—
Vinylidene chloride	0.5	0.4	1.1	1.0	—	—	—	—
Isoprene	0.7	—	33	—	1.0	—	0.3	—
Butadiene	4.5	4.0	$\infty$	—	—	1.0	0.3	—
Chloroprene	$\infty$	—	200	—	7.5	17.0	1.0	—
Vinyl acetate	0.02	—	—	—	—	—	—	1.0

reason the values in Table VI and VII may be affected by large errors; they merely illustrate the relative behavior of a given copolymer system.

**TABLE VII. Instantaneous Composition of Styrene Copolymers.**

Other monomer	$\sigma$	$\mu$	Mole % styrene in monomer mixture				
			5	25	50	75	90
			Mole % styrene units in copolymer				
Butadiene	0.5	1.4	4.5	19.5	39.5	59	81
Acrylonitrile	0.45	0.03	39	52	59.5	70.5	82
Methyl methacrylate	0.55	0.50	10	32	50	68	84
Vinylidene chloride	1.9	0.11	28	56	72	86	93
Maleic anhydride	0.03	0	50	50	50	50	50
Vinyl chloride	35	0.07	58	88	97	98	99
Vinyl acetate	55	0.01	74	94	98	99	99.5
$\alpha$ -Methylstyrene	2.00	0.47	12	40	66	84	97

It is evident that polymerization of individual monomers is a poor guide to their copolymerization behavior. Consider styrene and vinyl acetate monomers: styrene monomer is quite reactive, styrene free radical is stable and unreactive, vinyl acetate monomer is unreactive (compared to styrene), vinyl acetate free radical is unstable and reactive. Thus the self-polymerization of styrene (unreactive radical plus reactive monomer) and vinyl acetate (reactive radical plus unreactive monomer) may proceed at the same rate, but when the vinyl acetate monomer and styrene monomer must compete for the same free radical the greater reactivity of styrene monomer is apparent.

Copolymerization of styrene with another monomer is a useful tool in preparing polymers with an extremely wide range of properties and possible uses. Many of the improvements of polystyrene, such as high impact, heat, and chemical resistance have come about through the use of copolymers. It may be expected that much of the work done in the future to prepare new and more useful forms of polystyrene will be done in the field of copolymerization.

### Styrene-Based Plastics

The production of polystyrene has grown from less than 1,000,000 pounds in 1937 to over 300,000,000 pounds in 1952. Corresponding to this growth, the price has dropped from \$0.89 a pound in 1937 to \$0.325 a pound in 1953. This tremendous growth was first brought about by the great demand for styrene during World War II as a basic ingredient for GR-S synthetic rubber and then by the many applications for polystyrene developed during and after the war. Polystyrene is one of the least expensive thermoplastics. It is utilized in a tremendous and ever-increasing number of applications as a result of this low cost, its relative ease of fabrication, outstanding properties, and the continual development of improved types.

### MATERIALS

All commercial unmodified and modified polystyrenes suitable for injection molding and extrusion are available in granular form in a wide variety of particle sizes and shapes, in a wide range of colors, and with or without various kinds and amounts of internal and external lubrication treatments. Particle size becomes important when

colorants are added to the material by the fabricator. Very fine particles specifically designed for this purpose usually give the best pigment dispersion. Synthetic<sup>®</sup> waxes and zinc stearate are examples of materials which have been used as external lubricants to reduce the pressure losses incurred and improve the flow of the plastic as it travels through the molding machine. It may also facilitate removal of the molded part from the mold. Unlubricated polystyrene is normally used for extrusion where maximum mastication of the granules without slippage is desired. Unmodified polystyrene is available in a range from water-white crystal to all shades of transparent, translucent, and opaque colors. Modified polystyrenes of the high-impact types are available in only translucent and in opaque colors.

TABLE VIII. Physical Properties of Polystyrene.

Property	General-purpose unmodified (10)	High-impact (10)	Heat- and chemical-resistant (10)	Light-stabilized (7)
Specific gravity	1.04-1.065	0.98-1.1	1.05-1.11	1.05-1.07
Refractive index, $n_D$	1.59-1.60	—	1.57-1.60	1.59
Tensile strength, p.s.i.	5,000-9,000	3,500-7,000	7,000-12,000	6,000-7,200
Elongation, %	1-3.6	10-30	1.5-2.5	1.5-2.0
Modulus of elasticity in tension, 10 <sup>5</sup> p.s.i.	4-6	1.8-4.5	4-6	4.4-4.8
Compressive strength, p.s.i.	11,500-16,000	4,800-9,000	11,500-16,000	—
Flexural strength, p.s.i.	8,000-16,000	—	10,000-17,000	12,000-15,000
Impact strength, notched, ft.-lb./in. of notch	0.25-0.50	0.5-11	0.25-0.50	0.3-0.6
Hardness				
Rockwell M	65-90	20-70	65-90	68-80
Rockwell R	—	50-100	—	—
Thermal conductivity, 10 <sup>-4</sup> cal./ (sec.)(sq.cm.)(°C./cm.)	2.4-3.3	1.0-3.0	1.9-3.0	—
Specific heat, cal./ (°C.)(g.)	0.32	0.32-0.35	0.32-0.35	—
Thermal expansion, 10 <sup>-6</sup> /°C.	6-8	3.4-21	6-8	6-8
Heat distortion, °F.	160-210	148-200	190-235	168-175
Dielectric strength v/mil	500-700	300-600	400-600	—
Dielectric constant				
60 cycles	2.45-2.65	2.45-4.75	2.45-3.4	2.45-2.55
10 <sup>3</sup> cycles	2.4-2.65	2.4-4.5	2.4-3.2	—
10 <sup>6</sup> cycles	2.4-2.65	2.4-3.8	2.4-3.1	2.45-2.55
Dissipation factor				
60 cycles	0.0001-0.0003	0.0003-0.02	0.0005-0.003	0.0001-0.0003
10 <sup>3</sup> cycles	0.0001-0.0003	0.0004-0.02	0.0005-0.003	—
10 <sup>6</sup> cycles	0.0001-0.0004	0.0004-0.02	0.0005-0.005	0.0001-0.0004
Arc resistance, sec.	60-135	20-100	60-135	—
Water absorption, 24 hr.	0.03-0.05	0.05-0.40	0.1-0.55	—
Burning rate	Slow	Slow	Slow	—

The following polystyrene formulations have been covered by A.S.T.M. Specification D703-49T (2): Type 1, a general-purpose compound of unmodified polystyrene which may contain small amounts of lubricant; type 2, a lubricated general-purpose polystyrene compound; type 3, a polystyrene compound characterized by improved heat distortion temperature. Several other types have been developed with improved properties. Of these modified polystyrenes, those exhibiting improved heat distortion temperatures, solvent resistance, impact strength, and light stability

have found extensive commercial use. Detailed properties of these materials may be found in Table VIII.

**General-Purpose, Unmodified Polystyrene.** Pure, unmodified polystyrene enjoys the largest use of all the polystyrene types available. Its properties are well covered in Table VIII and in the section "Physical Properties of Polystyrene."

**High-Impact Polystyrene.** Modified polystyrenes exhibiting greatly improved impact strength and elongation have found the widest use of the various modified types. These materials are either mechanical mixtures of polystyrene and rubber or styrene-rubber copolymers. The amount of rubber used is generally between 2 and 20%, and it may be natural, GR-S, or GR-N rubber. Figure 8 illustrates typical stress-strain relationships for unmodified and high-impact polystyrene. The excellent

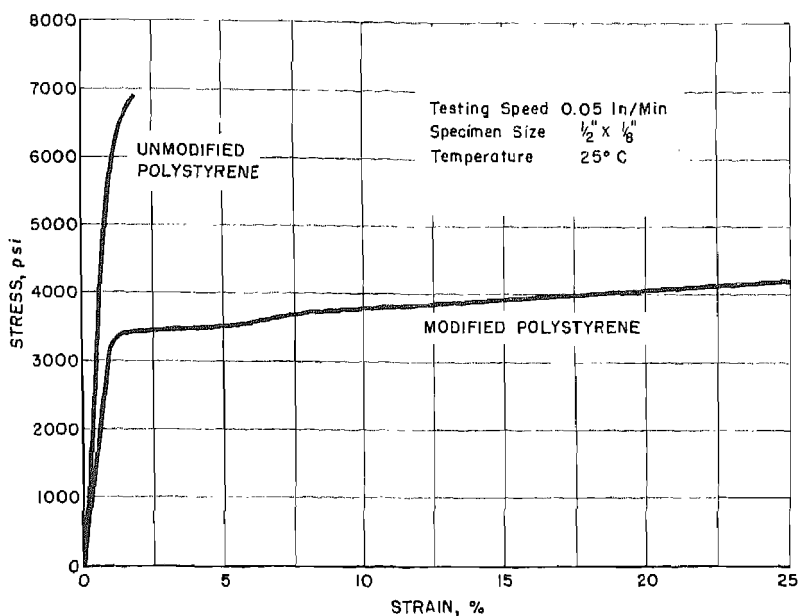


Fig. 8. Stress-strain relationships for unmodified and high-impact polystyrene.

elongation of high impact polystyrene is accompanied by notched impact strengths of 0.5–11 ft.-lb. per inch of notch. Compared to unmodified polystyrene, these materials possess reduced tendency to craze, exhibit less satisfactory aging and weathering properties, and permit the use of metal inserts in the mold. They may be mixed with unmodified polystyrene to obtain intermediate physical properties. They may be obtained in granular form for injection molding and extrusion as well as extruded sheet suitable for vacuum forming. High-impact sheet is available in a variety of sizes; with thicknesses up to 0.500 in.; in a wide range of colors; and with mirror, matte, pebble, or patterned surface finish. It is also available in formulations exhibiting varying degrees of impact strength, chemical resistance, and self-extinguishing properties.

**Heat-Resistant Polystyrene.** Modified polystyrenes with heat distortion temperatures of over 200°F. have been developed by copolymerizing styrene with other monomers or by polymerization techniques resulting in polymers with only minute traces of monomer or volatile solvents. Figure 9 illustrates the effect of several co-

polymer systems on the heat distortion temperature of polystyrene. Materials with improved heat distortion temperature have been designed for use in applications such as radio cabinets where high temperatures are developed. Usually improvement of heat distortion temperatures has been achieved at the expense of ease of molding since higher molding temperatures and pressures are required.

**Solvent-Resistant or Chemical-Resistant Polystyrene.** Copolymers of styrene with 5–50% acrylonitrile or related monomers exhibit greatly improved resistance to chemical attack by many reagents and may have tensile strengths and elongations slightly greater than unmodified polystyrene. They may be swollen but not dissolved by aromatic compounds, and they are soluble in ketones. Applications requiring resistance to motor oils, some gasolines and kerosenes, and normal heptane are examples of where these materials may be used; also specific chemical resistance tests should be conducted for each application prior to production of a molded article.

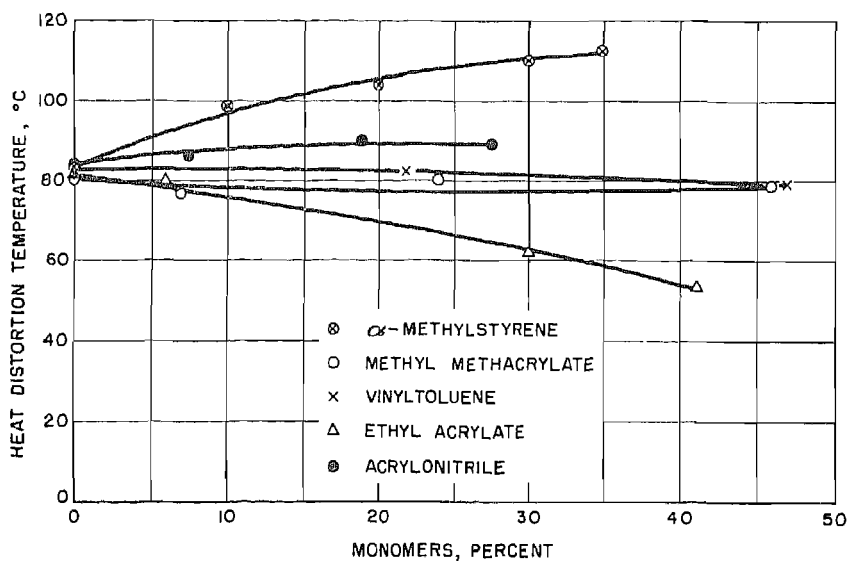


Fig. 9. Effect of several styrene copolymer systems on heat distortion temperature.

Styrene-acrylonitrile copolymers tend to be more hygroscopic than unmodified polystyrene and should be preheated at 170–190°F. for a half hour prior to molding to insure obtaining maximum physical properties. High molding temperatures and pressures are required to fabricate these materials. They may have a slight yellow cast and are not compatible with unmodified polystyrene.

**Light-Stabilized Polystyrene.** Stabilizing agents may be incorporated into polystyrene to enable it to withstand much longer exposure to indoor lighting fixtures without yellowing or showing a reduction of physical properties. These materials are available in crystal, translucent, and opaque whites. This type of polystyrene, as well as all other types, is not recommended for outdoor exposure to sunlight. Stabilization of polystyrene to avoid the effects of light may best be accomplished through addition of a series of saturated aliphatic and cyclic amines and amino alcohols. Addition of 1% of one or a number of amines with ionization constants greater than  $10^{-8}$  increases several times the nonyellowing life of polystyrene exposed to indoor lighting (25).



**Expanded Plastics.** Expanded polystyrene foams have found considerable use in recent years. These foams are produced by introducing a foaming agent, such as methyl chloride under high pressure, into molten polystyrene, which is extruded as logs or planks of various sizes. Polystyrene foams of this type consist of many tiny noninterconnected cells. These foams have low densities, low thermal conductivity, and good structural strength, and form excellent water vapor barriers. Table IX illustrates the properties of a typical expanded polystyrene foam. Expanded polystyrene foams with self-extinguishing characteristics are also available.

**TABLE IX. Properties of Expanded Polystyrene Foam.<sup>a</sup>**

Properties	Density, lb./cu.ft.		
	1.3	1.6	2.0
<u>Mechanical (77°F.)</u>			
Compressive yield strength, p.s.i.	10-20	15-25	25-35
Tensile strength, p.s.i.	30-45	50-70	80-100
Shear strength, p.s.i.	15-25	25-35	35-45
Compressive modulus, p.s.i.	450-1100	750-1350	1150-1750
Bending modulus, p.s.i.	200-750	650-1200	1200-1900
Impact strength, in.-lb./in. of width	0.5-1.2	1.1-1.8	2.1-2.7
	(3/8 in. x 1/2 in. section)		
<u>Thermal</u>			
Thermal conductivity, B.t.u./(hr.)(sq.ft.)(°F./in.)	0.23-0.30 at mean temperature of 40°F.		
Linear thermal coefficient of expansion	2-5 × 10 <sup>5</sup> /°F. between 320 and 500°F.		
Specific heat, B.t.u./(lb.)(°F.) at 40°F.	0.27		
Heat distortion, °F.	175 maximum for continuous service		
Water absorption	<6% by volume, <0.1 lb./sq.ft. of area		
Water vapor transmission, grains/(hr.)(sq.ft.)(in. Hg/in.)	1.5-3.0		
<u>Electrical</u>			
Dielectric constant	<1.05 from 10 <sup>2</sup> to 10 <sup>6</sup> cycles/sec.		
Power factor	<0.0002 from 10 <sup>3</sup> to 10 <sup>8</sup> cycles/sec.		

<sup>a</sup> Data for Styrofoam, an expanded polystyrene produced by Dow Chemical Company.

These materials may be easily cut and worked into almost any desired shape with conventional woodworking tools. Hot-wire cutting is a unique method of fabrication involving the melting and shrinking of the cell structure. Through proper selection of adhesives and techniques, these foams may be bonded to wood, metal, masonry, cloth, paper, glass, themselves, and some other plastics. They may also be painted to any desired color. The properties of these materials have led to their widespread use in the low-temperature insulation of refrigerated rooms and vehicles, as a buoyancy material for small boats, and for floral, display, and novelty applications.

Recently, foaming-in-place polystyrenes, containing a gas, have become available. They are supplied in granular form which requires less storage space than foams supplied as logs and planks. When these granules are exposed to temperatures of 230-270°F., they expand to many times their original size. Hot air, water, or 10-30 p.s.i. dry steam may be used as the heating medium. All three of these methods may be used to heat the mold platens; however, steam may be fed directly to the granules in the mold cavity to accomplish foaming. The properties and possible applications for

foaming-in-place polystyrenes are the same as for foams supplied as logs and planks. The primary advantage of foaming-in-place polystyrenes is that they may be molded to fit the contours of insulation area or any other shape in a single operation.

#### PHYSICAL PROPERTIES OF POLYSTYRENE

Polystyrene may be described as a hard, rigid, crystal-clear thermoplastic of low specific gravity, completely free of odor and taste. Its adaptability for injection and extrusion molding combined with its low cost and specific gravity results in molded parts of very low unit cost. Polystyrene exhibits excellent physical and electrical properties, selective resistance to chemical attack, very low moisture absorption, and extensive color possibilities. It is very stable at fabrication temperatures and retains good physical properties at all temperatures below the heat distortion temperature.

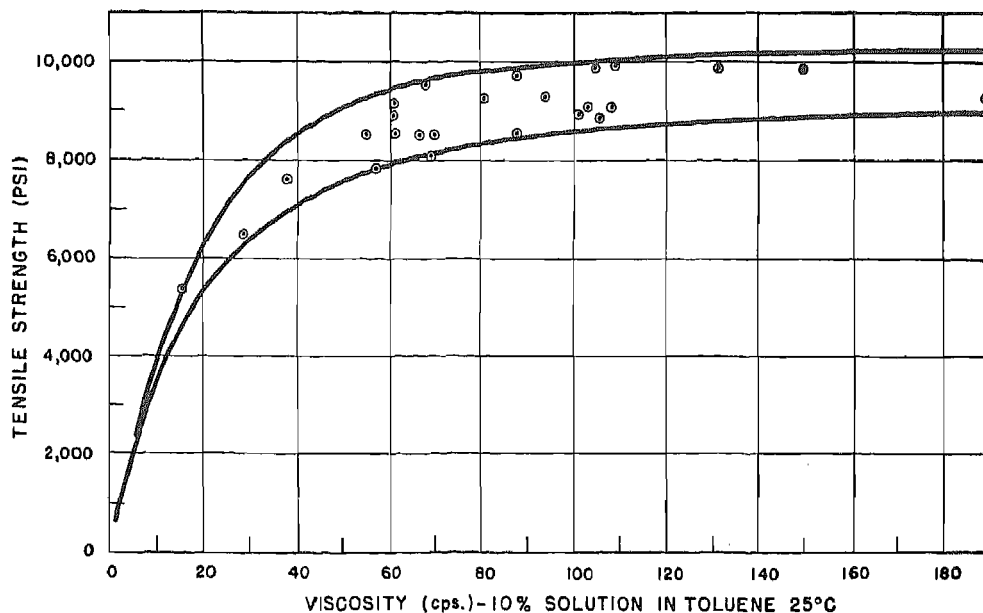


Fig. 10. Tensile strength of polystyrene as a function of its molecular weight (in terms of 10% solution viscosity in toluene at 25°C.). The solid lines are drawn as an envelope to make the general behavior more evident (4, p. 452).

The physical properties of polystyrene may be affected by many factors, among them the method and conditions of polymerization, molecular construction of the polymer, degree of orientation of the polymer after fabrication, fabrication techniques, temperature at which properties are measured, test specimen size and shape, and the impurities present in the monomer and polymer. Polystyrene is not a sharply defined material chemically. Such things as average molecular weight, molecular weight distribution, chain geometry, and volatile content can vary tremendously. Polystyrene can exist in many different states mainly determined by orientation of polymer chains and by nonequilibrium configurations frozen into the material when it is cooled rapidly. On this basis Table VIII reflects a wide range in each physical property.

Figure 10 illustrates the dependence of tensile strength of unmodified polystyrene

on molecular weight or degree of polymerization in terms of 10% solution viscosity. The heat distortion temperature and impact strengths are also dependent on the degree of polymerization and, if plotted against solution viscosity, would follow the same pattern as Figure 10.

The presence of impurities in styrene monomer adversely affects the physical properties of polystyrene. Most impurities, such as ethylbenzene, sulfur (over 0.2 p.p.m.), and aldehydes tend to reduce the molecular weight. Ethylbenzene, unreacted styrene monomer, and other volatile materials tend to evaporate from polystyrene and may cause blushing or crazing. This reduces mechanical strength and impairs appearance. Volatiles in the polymer also serve to plasticize the polymer, reducing its heat distortion temperature and other physical properties. Since many of the physical properties of polystyrene are dependent on the molecular weight and freedom from entrapped volatile materials, it becomes obvious that control of impurities is essential for the consistent production of polymers with desired properties.

Molecular oxygen from the air above the polymerizing mass may react with the monomer to form aldehydes and peroxides, and it may also react with growing polymer chains. Thus, it can function both as a catalyst and as an inhibitor. Oxygen, if present in sufficient amounts, will cause styrene monomer to become yellow. It has been suggested that oxygen in the polymer chain is a weak link and facilitates thermal degradation of the polymer. These factors have led to the use of nitrogen atmospheres above polymerization reactions.

During injection molding the high shearing forces resulting from hot polymer (300–400°F.) being forced into a cool mold (140–170°F.) cause orientation of the polymer molecules in the direction of flow. Rapid cooling of the part freezes the orientational strains into the part. If this orientation is severe enough, the product will have highly directional physical properties; the part will be brittle and easily broken, and its tendency to craze will be increased. The tendency of these strains to relax may lower the heat distortion temperature. It is desirable to employ molding conditions to give minimum amounts of these strains and to anneal parts whose applications require optimum physical properties.

Higher strengths are usually obtained at higher molding pressures and lower molding temperatures. The magnitude of variation will depend on the polymer used and the characteristics of the injection molding machine, but the general effect will be the same. In practice the molding conditions employed are often those giving the best appearance, speed, and ease of molding, and they are not necessarily those giving optimum strength. One of the outstanding properties of polystyrene is that it can be fabricated over a wide range of conditions and retain adequate physical properties.

The variation of physical properties credited to orientation and molding conditions is somewhat of a cause-and-effect relationship. By varying the molding conditions various degrees of orientation can be obtained, although not eliminated. The extent of orientation determines the effect on physical properties.

Test specimens of different dimensions and shapes will give different test results for tensile strength, impact strength, and heat distortion. Data seem to indicate that for a given cross-sectional area the strength increases as the perimeter increases, or, in other words, the thinner the molding, the higher the relative tensile strength, assuming equivalent fabrication techniques.

Temperature has a marked effect on most of the physical properties. As the temperature increases, tensile strength drops, elongation increases, modulus of elastic-

ity drops, flexural strength decreases, but impact strength remains essentially unchanged. High-impact polystyrenes behave differently; the impact strength and elongation increase at higher temperatures and decrease as the temperature is lowered. At  $-40^{\circ}\text{F}$ . these properties are nearly the same as those of unmodified polystyrene. It may be seen that the temperature at which a molded object is to be used plays an important role on the physical properties it will exhibit in use.

The effect of light on polystyrene can be summarized as follows: (1) Polystyrene yellows in sunlight. (2) This limits the use of polystyrene in outdoor applications. (3) The color change of a particular polystyrene can be approximately checked by use of a carbon arc exposure test. (4) The changes which occur with polystyrene are not large compared to some other plastics. Light stabilized polystyrenes have been specially developed for use in indoor lighting fixtures.

There is no odor or taste to polystyrene moldings, and they may be used in contact with food and the skin without danger. There is no evidence to indicate that polystyrene free from addition agents and large amounts of low-molecular-weight polymer presents any health hazard from oral ingestion or skin contact. The fumes from heated polystyrene may be disagreeable and for that reason should be controlled.

Owing to the high surface and volume resistivity of polystyrene, the dissipation of static charges is very slow. The use of some polishes, waxes, and soaps will help prevent static buildup and facilitate static charge dissipation. All known destaticizers are water-soluble and are removed by washing molded parts. The display or storage of polystyrene parts may result in accumulation of dust, lint, or dirt due to surface static charges on the object. There is no commercial formulation completely free from electrostatic difficulties.

Crazing, or the formation of fine, hair-like cracks, sometimes appears and weakens polystyrene moldings. They are due to local tensile failures and may be caused by excessive externally applied forces, relaxation of strains molded into the article during fabrication, thermal expansion, evaporation of volatile material from the part, or chemical and solvent attack. Crazing may be minimized by annealing molded parts to reduce the strains molded into the piece. The volatile content can be reduced through polymerization techniques.

Orientational stresses are incurred during the injection-molding process in the direction of plastic flow. They strengthen the part in the direction of orientation, but weaken it at right angles to the flow. In actual use, parts craze at right angles to the applied stress and along the lines of least strength. Tests have indicated that the critical elongation (elongation required to produce crazing) for injection molded parts stressed in "across flow" direction compares very well with that for compression molded parts where orientational stresses are nil. The figures quoted represent work done with compression molded parts and can be translated into useful values of tensile stress below which even the weakest portion of the injection molded part will perform satisfactorily, but above which it may craze.

The instantaneous critical elongation of unmodified polystyrene, or the elongation required to cause crazing, is 0.75% in air at  $75^{\circ}\text{F}$ . If the material is held at constant strain at  $75^{\circ}\text{F}$ . for prolonged periods, the critical elongation drops and comes to an equilibrium value of 0.33% in about 50 hours. Many reagents and materials when in contact with unmodified polystyrene cause a much more rapid and severe decrease in the elongation required to cause crazing. Table X (8) illustrates the equilibrium critical elongation and the corresponding stress for several materials when used in

contact with unmodified polystyrene. Higher temperatures reduce the equilibrium critical elongation obtained and the time required to reach this equilibrium. This time also depends on the size and configuration of the piece. The effect of contact with such reagents, whether intermittent or continuous, is cumulative with the critical elongation determined by the total contact time.

**TABLE X. Effect of Several Reagents on Critical Elongation of Unmodified Polystyrene at 75°F.**

Reagent	Minimum equilibrium	
	Critical elongation, %	Critical stress, p.s.i.
Water	0.33	1500
Air	0.33	1500
<i>n</i> -Heptane	0.01+	50
Cream	0.10	450
Natural hair oil	0.10	450
Butter	0.10	450
Methanol or ethylalcohol	0.23	1000
Various kerosenes	0.04-0.05	200-250

This demonstrates that unmodified injection-molded polystyrene parts can withstand stresses of 7,000 p.s.i. in the direction of plastic flow for but a few seconds without crazing failure. When stressed in the "across flow" direction, the part cannot withstand stresses above 1,500 p.s.i. indefinitely. This represents the maximum allowable stress in a molded part without crazing, since crazing always occurs in the weakest part of the mold or along the direction of plastic flow. This maximum indefinite load is reduced when the temperature is raised and/or other reagents are brought in contact with the plastic. The development of chemical-resistant polystyrene has resulted in parts with about three times the critical elongation of unmodified polystyrene under identical conditions.

Chemical resistance of polystyrene is limited by chemical reaction and by the solvent properties of the polymer. Reactions characteristic of the phenyl group, such as chlorination, nitration, Friedel-Crafts, and sulfonation, may occur; they result in chain rupture and lowered chemical resistance. The literature gives comprehensive data on the resistance of polystyrene to many materials as determined by A.S.T.M. methods. In general, it may be stated that polystyrene formulations are unaffected by weak acids and weak and strong alkalies, are attacked by oxidizing acids, and are soluble in aromatic and chlorinated hydrocarbons. Specific chemical resistance tests should be conducted for each application.

The use of plasticizers and fillers with polystyrene molding and extrusion formulations has not been very successful. Fillers of types normally employed with thermoplastics do not reinforce polystyrene but actually weaken the material. The use of plasticizers with polystyrene improves the ease of fabrication but decreases the heat distortion temperature and does not give stronger or more extensible products. The recent development of fibrous-glass-reinforced polystyrene suitable for injection molding and extrusion on conventional equipment has opened a new approach to the subject of fillers. These formulations have heat distortion temperatures above 200°F., tensile strengths up to 10,500 p.s.i., and specific gravities from 1.12 to 1.30.

## RHEOLOGICAL PROPERTIES OF POLYSTYRENE

Many properties of polystyrene, such as tensile strength, impact strength, heat distortion temperature, and optimum molding conditions, may be understood in terms of its fundamental rheological properties (ref. 4, pp. 574-608; ref. 17).

Polystyrene is a hard, brittle material at room temperature. As the temperature is raised, it softens and assumes rubber-like properties, and at still higher temperatures it behaves more as a highly viscous liquid. Its flow characteristics are like a Newtonian liquid at low shearing stresses and a non-Newtonian liquid at higher shearing stresses. The rheological properties of polystyrene change smoothly and continuously as the material is heated beyond its solid-liquid transition point. For polystyrene this is about at its A.S.T.M. heat distortion temperature of 80°C.

The deformation of polystyrene under stress can be analyzed in terms of three deformation mechanisms: ordinary elasticity, high elasticity, and viscous flow. Ordinary elastic deformation is instantaneous, recoverable, very slightly increased with increasing temperature, and relatively independent of molecular weight. The ordinary elasticity of polystyrene at room temperature results in elongations of 1.0-2.0% at the breaking point. The highly elastic portion of deformation is the result of uncoiling or stretching out the polymer chains and is recoverable and time-dependent. The rate of highly elastic deformation increases markedly at higher temperatures and is characterized by an orientation or relaxation time depending exponentially on the temperature. Activation energies of 60-100 kg.-cal. per mole are required. The modulus of high elasticity increases slightly with temperature and is inversely proportional to the molecular weight of the polymer. Viscous flow results from polymer molecules moving past one another and is not recoverable. It is characterized by the viscosity of the polymer and becomes important above the heat distortion temperature. The viscosity is highly temperature-dependent, decreasing with increasing temperatures. The degree of dependence of viscosity upon temperature is expressed by

TABLE XI. Relative Contributions of Deformation Mechanisms in Hypothetical Tensile Creep Experiment.

Temp. of experiment, °C.	Total deformation per unit stress at 10 min.	Fraction contributed by		
		Ordinary elasticity	High elasticity	Viscous flow
30	$4 \times 10^{-11}$	1.000	—	—
40	4.01	0.998	—	0.002
50	4.08	0.981	—	0.019
60	4.58	0.874	0.001	0.125
70	8.25	0.485	0.048	0.467
80	$4.93 \times 10^{-10}$	0.081	0.513	0.406
85	$2.36 \times 10^{-9}$	0.017	0.790	0.193
90	$1.39 \times 10^{-8}$	0.003	0.925	0.072
95	8.49	—	0.973	0.027
100	$4.50 \times 10^{-7}$	—	0.989	0.011
110	$1.45 \times 10^{-6}$	—	0.986	0.014
120	1.51	—	0.947	0.053
130	1.72	—	0.833	0.167
140	2.36	—	0.606	0.394
150	4.60	—	0.311	0.689
200	$4.77 \times 10^{-4}$	—	0.003	0.997

Source: Ref. 4, p. 605.

the activation energy of viscous flow, which ranges from about 22 kg.-cal. per mole at temperatures in the range required for injection molding up to more than 100 kg.-cal. per mole as the temperature drops to the neighborhood of the heat distortion temperature. Table XI indicates the relative contributions of these three mechanisms in a hypothetical tensile creep experiment conducted with unmodified polystyrene at a series of temperatures.

The practical applications of these concepts fall into two main classes: the fabrication conditions required to mold polystyrene successfully, and the behavior of the molded parts in service. At typical injection-molding temperatures of over 400°F. most of the deformation comes from viscous flow. As the viscosity decreases with rising temperature, it becomes easier to force the plastic through the injection-molding

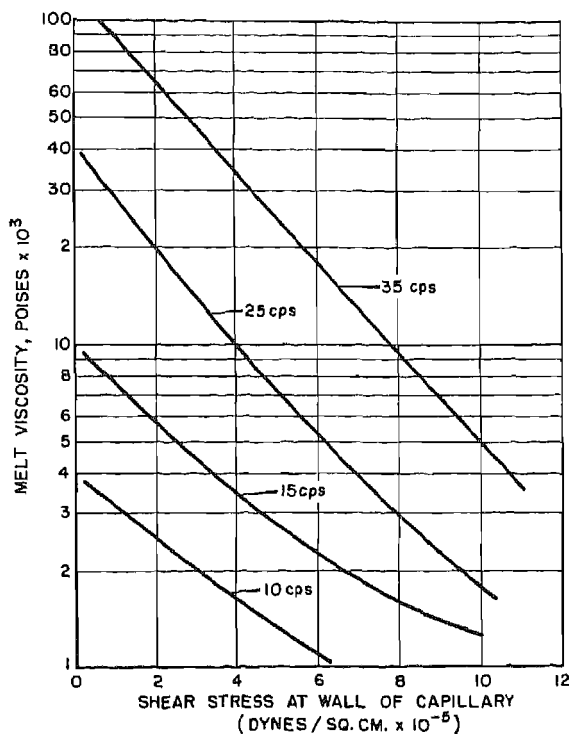


Fig. 11. Effect of shearing force on the melt viscosity of polystyrene of different molecular weights at 440°F. (Molecular weight in terms of 10% solution viscosity in toluene.)

machine and into the mold. The accompanying highly elastic deformation provides an additional complication, however. The polymer chains are partially uncoiled and oriented as the hot plastic flows through the channels of the machine and mold. Through the rapid chilling occurring in the relatively cool mold, some amount of this orientation is frozen in. This residual deformation may be relieved if the molded object is later heated above its heat distortion temperature, but this results in warping the piece.

In the range of temperatures and pressures required for injection molding, polystyrene behaves as a non-Newtonian liquid. Figure 11 illustrates this sensitivity of

melt viscosity to changes in the pressure gradient. Figure 12 relates the melt viscosity at zero shear with molecular weight of the polymer at several temperatures.

High-impact polystyrenes present a different picture. At room temperature they

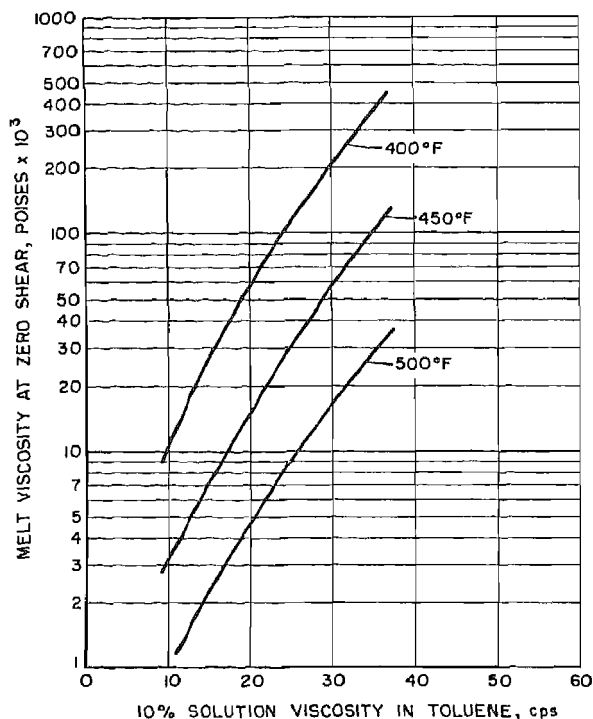


Fig. 12. Effect of molecular weight of polystyrene on melt viscosity at several temperatures. (Molecular weight in terms of 10% solution viscosity.)

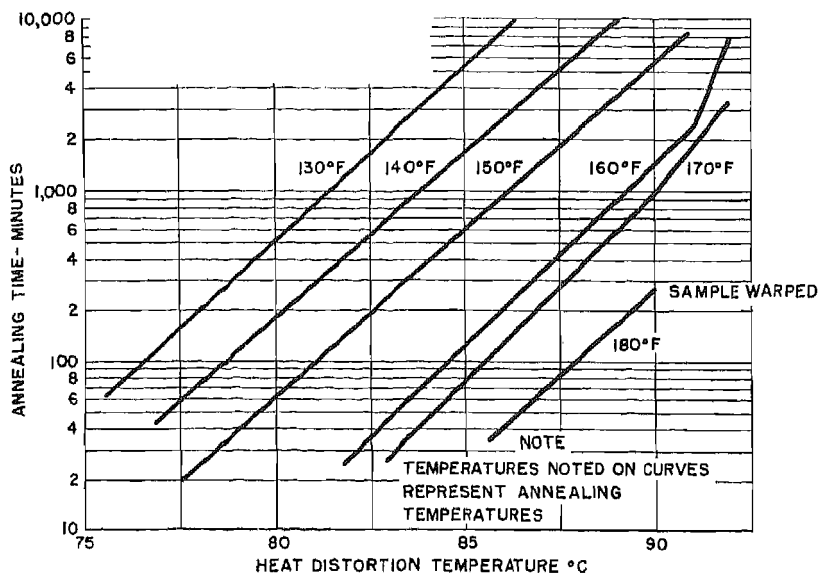


Fig. 13. Effect of annealing on heat distortion temperature of polystyrene moldings.



have nearly the same ordinary elasticity as unmodified polystyrene at low stresses, while at higher stresses they do not fail as soon but exhibit a yield point and continue to lengthen up to 30% before failure. From the yield point to failure, deformation is due to viscous flow which is nonrecoverable. As the temperature is increased, the relative contributions of the deformation mechanisms follow the same pattern as with unmodified polystyrene. This ability of high-impact polystyrene to lengthen well beyond its elastic limit without failure accounts for its toughness compared to unmodified polystyrene. It is the basis for its many applications.

The use of molded parts is limited to temperatures below the heat distortion point. The heat distortion temperature may be defined as the temperature at which a predetermined amount of deformation occurs when the part is subjected to a given load for a specified length of time. It depends upon the conditions of the test, including specimen size and shape, rate of heating, and the load imposed. Various testing conditions result in different values for the heat distortion temperature.

Internal strains in molded parts may lower heat distortion temperatures. These strains may be classified as follows: (1) thermally induced cooling strains analogous to those found in glass; (2) strains induced by local heating during machining or other mechanical operations; (3) unrelaxed orientation due to high elastic deformation incurred during fabrication; (4) volumetric strains due to molecules in the molded part not being in their equilibrium configuration.

Annealing can remove a large percentage of these strains. This can result in parts with higher heat distortion temperatures, less tendency to craze, and better physical properties. Figure 13 illustrates the effect on A.S.T.M. heat distortion temperature of different annealing schedules.

#### FABRICATION OF POLYSTYRENE

The fabrication of polystyrene into a desired object usually involves a combination of temperature, time, pressure, and sometimes removal of solvent (4). Polystyrene in granular form is ideally suitable for extrusion and injection molding, while extruded high impact sheet is widely used in vacuum forming. Compression molding of polystyrene is quite limited because of its inherent high cost resulting from long heating and cooling cycles. See also *Plastics*.

**Injection Molding.** Today at least 85% of the polystyrene produced is fabricated by injection molding. This is due to the ease with which polystyrene can be molded over a wide range of operating conditions (up to 600°F. and 30,000 p.s.i.), the speed of injection molding (cycles as short as 15 sec.), the ready availability from the manufacturers of free-flowing granules designed for injection molding, and the excellent heat stability of polystyrene at high temperatures for relatively long periods of time. The greatest limitation to the injection-molding process is the investment required for an injection-molding machine (up to \$100,000) compared to the size of the article produced (10–12 lb.). With experience, careful mold design, and knowledge of injection molding techniques and machine tool operations, the advantages of injection-molding outweigh the limitations.

The technology of injection molding of polystyrene has moved in the direction of pressure conservation as the plastic flows through the heating cylinder, nozzle, sprue, and runners. By minimizing the pressure losses through the system, more pressure is available to force the plastic through the gate and into the mold more rapidly. In other words, nozzles, sprue, and runners should be designed to minimize pressure losses.

Restricted or pin-point gating has been advantageously used in the molding of many objects. Owing to the small volume of plastic in the gate area, it chills rapidly, sealing the plastic in the mold, usually before the molded object becomes rigid. This enables

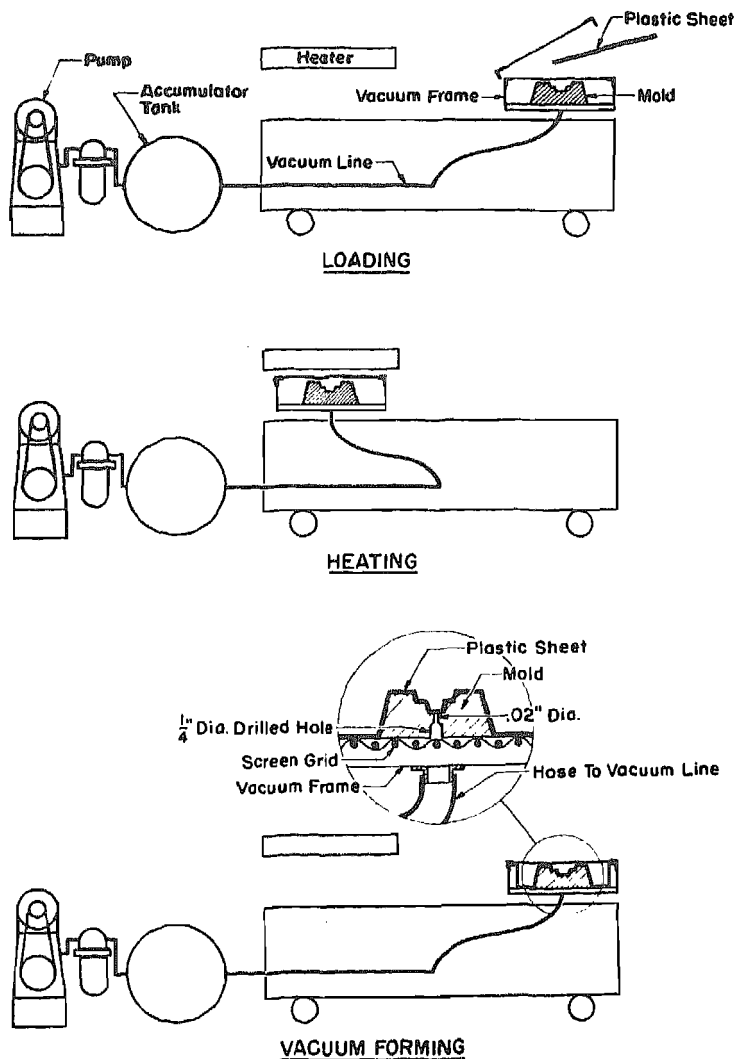


Fig. 14. Vacuum forming process for high-impact polystyrene sheet.

the injection ram to be withdrawn earlier in the cycle, preventing it from packing or overfilling the mold. Restricted gating also provides a means of controlling plastic flow in the cavity since by varying gate dimensions the pressure drop through the gate can be changed, thus varying the rate of fill. This leads to balanced gating in multi-cavity molds where it is desirable to have each cavity fill at the same rate to prevent forcing too much plastic into one cavity and not enough into another. By varying the gate dimensions for each cavity, this can be accomplished.

The use of weigh feeding devices and mold temperature control units has improved

the quality of injection-molded polystyrene parts. Weigh feeding devices meter the exact weight of granules required to just fill the mold. The injection ram is operated to the mechanical limit of its travel and displaces the same amount of plastic from the nozzle and into the mold during each cycle. This allows the use of maximum machine injection pressure and avoids the overfilling of the mold that often occurs with older types of volumetric feeding mechanisms. This reduces the possibility of the part cracking on ejection from the mold and reduces the orientation strains molded into the part, considerably improving its quality. Mold temperature control units maintain the mold at a constant temperature, thus improving the flow of plastic, increasing the strength of weld lines, reducing molded-in strains, and improving the surface finish obtained.

**Extrusion.** Extrusion of polystyrene is one of the most economical methods of fabrication since it is a continuous process with relatively inexpensive equipment. Roughly 10% of the polystyrene produced is fabricated by extrusion. Usual extrusion practice involves reducing the size of the molten section as it leaves the die by 15–20% by operating the take-away equipment at a rate faster than the rate of plastic extrusion. This is a means of size control and requires constant extrusion (less than 2% variation) and take-away rates. Good extrusion and take-away equipment should be capable of producing at commercial rates a section 6 in. wide with tolerances of less than  $\frac{1}{16}$  in.

**Compression Molding.** Compression molding of polystyrene accounts for around 5% of the polystyrene produced. The high cost of compression molding of polystyrene is justified in applications requiring extreme precision, very heavy sections, or excessively large areas. New equipment has been developed which frictionally preheats the polystyrene granules and feeds them directly to the mold. This may well eliminate a portion of the molding cycle, possibly offering a more encouraging future for compression molding of polystyrene. High-frequency heating is not effective because of the very low electrical losses in the polystyrenes.

**Forming Polystyrene Sheet.** Large quantities of extruded high-impact polystyrene sheet are fabricated by vacuum forming techniques. One of the common methods calls for clamping the sheet in a frame above a large box containing the mold. The sheet is then heated to the proper temperature (325–350°F.) with a radiant heater placed above the sheet. At this point a vacuum is drawn on the box, and the sheet acts as a flexible diaphragm and is rapidly sucked into or over the desired form. Figure 14 illustrates this process.

A second method vacuum-forms the sheet as it is extruded from a conventional extruder. This method is especially adapted to small items such as dishes and trays. Portable molds are used to which suitable vacuum and cooling water lines may be connected. Forming operations are all characterized by relatively low costs for equipment and molds compared to injection molding and extrusion.

**Orientation of Polystyrene.** When polystyrene is heated above its heat distortion temperature (about 82°C.) and stretched under carefully controlled conditions, considerable orientation of the polymer molecules can be attained. If the oriented material is cooled in its stretched state, the resulting material will exhibit greatly improved physical properties in the direction of stretch. Tensile strengths may be more than doubled and elongations at failure increased ten to fifteen times. Bidirectional stretching (stretching the hot plastic both longitudinally and transversely) will produce oriented polystyrene with improved properties in all directions. For films 0.005

in. thick, longitudinal strengths of 9,000–10,000 p.s.i. and lateral tensile strengths of 10,000–13,000 p.s.i. have been produced.

The improvement in properties obtained through orientation has led to the use of oriented polystyrene as bristles in brooms, dusters, scrub brushes, and other utility brushes. Bilaterally oriented polystyrene has been produced as crystal-clear film as thin as 0.001 in. for use in electrical and packaging applications.

#### USES OF POLYSTYRENE

The problem of translating the properties of polystyrene into useful applications can only be accomplished through careful product design. It is necessary to choose the proper type of polystyrene to obtain the properties desired in the molded part, and the properties of the polystyrene must be considered when building the mold to account for mold shrinkage, factors influencing dimensional tolerances, and the proper use of ribs, fillets, draft angles, taper, and undercuts. Finally, a knowledge of fabrication techniques is essential to obtain a part with the optimum physical properties to be expected from the type of polystyrene used.

The uses of polystyrene are limited in some applications where prolonged exposure to sunlight and atmospheric conditions is required since it will turn yellow with a corresponding drop in physical properties. Even with the development of heat-resistant types, exposure to temperatures over 220°F. excludes the use of polystyrene.

The uses and applications of polystyrene have become very diverse, especially with the development of new types of polystyrene with properties designed to make them useful in new applications. Today we find polystyrene used in toys, wall tile, refrigerator parts, radio cabinets, television masks, room air conditioner cabinets, bristles for brushes, housewares of all types, containers and ornamental boxes, indoor light diffusers, lenses for low power instruments, storage battery cases, and many other articles.

To illustrate how the development of new types of polystyrene has affected its use, consider the manufacture of household refrigerators. In 1953 over 5,000,000 units were produced containing about 12 lb. of polystyrene each for a total of more than 45,000,000 lb. of polystyrene consumed during the year. Until the development of a polystyrene with high impact strength, such applications would be impossible. Of the estimated 8,000,000 radio receivers (table, clock, portable) produced in 1953, about 4,000,000 used polystyrene cabinets consuming more than 7,200,000 lb. of polystyrene. Such use was impossible until the development of heat-resistant materials capable of withstanding the temperatures developed inside radio cabinets.

Items produced from unmodified polystyrene include toys, kitchenware, a variety of refrigerator and freezer parts, as well as containers for ice cream and cottage cheese. Of considerable interest is the recent color styling of polystyrene wall tile colors for interior decoration schemes. Many other applications also take advantage of the almost unlimited color possibilities of polystyrene.

#### Styrene-Based Latexes

In recent years styrene-based resin latexes have undergone tremendous growth. The majority of these latexes are styrene-butadiene copolymers. Figure 15 illustrates the range of styrene-butadiene latexes possible and their general fields of application.

In 1952 over 40,000,000 lb. of styrene was consumed in the production of latex-based paints alone.

Styrene-based latexes are colloidal dispersions, of particle size from 10 to 200  $m\mu$ , in an aqueous medium (4, pp. 857-60). They are relatively odor-free, contain little or no solvent, and can be prepared with high solids content at a lower viscosity than corresponding solutions. Styrene contributes hardness, strength, and chemical resistance to the films deposited from the latex.

Styrene latexes can be classified as follows: (1) *Film formers*. Styrene-butadiene latexes containing 50-75% styrene which, upon evaporation of the water phase, deposit particles which coalesce upon drying to form a continuous film. (2) *Non-*

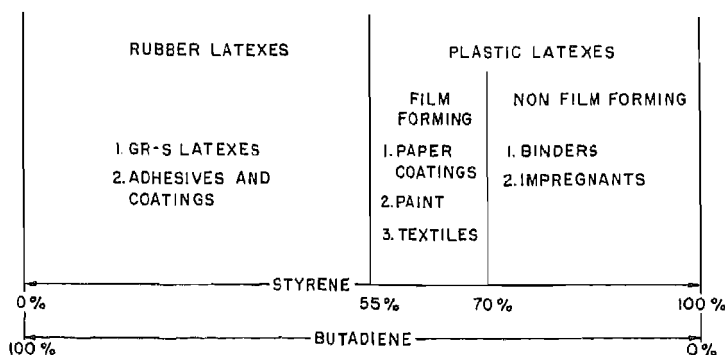


Fig. 15. Styrene-butadiene copolymer latexes and their uses.

*film formers*. High-styrene latexes which, upon evaporation of the water phase, deposit fine powders which have no binding properties. (3) Latexes which form very tacky films requiring vulcanization to give useful properties. Standard GR-S rubber latexes (Type II) are representative of these materials.

#### FILM-FORMING LATEXES

The majority of film-forming latexes are styrene-butadiene copolymers containing 50-70% styrene. These latexes have found their largest use in the formulation of latex paints which exhibit improved properties over other types for certain applications. See also Vol. 9, p. 795.

Latex-based paints may be classified into four types (11,12): (1) primer sealer paints, (2) interior paints, (3) exterior masonry paint, and (4) texture paints. The development of these paints has done much to popularize the "do it yourself" trend in home decorating and construction. They have increased the amount of painting done and, consequently, the total paint sales. This becomes more apparent when one considers the properties of these paints: lack of toxicity; ease of application with brush or roller; professional appearance of finished job; ease of cleaning rollers, brushes, and hands with soap and water; rapid drying, very little paint odor; ease of washing soiled painted surfaces; and excellent self-sealing. In addition, they do not putrefy on storage and can be packaged at proper consistency for application without further dilution. Since latex-based paints employ water as the volatile vehicle, care should be taken to avoid outdoor storage when there is a possibility of freezing. Oil-based paints depend on chemical oxidation of the oil, varnish, or alkyd to form a solid film, a

time-consuming and temperature-dependent process sometimes taking as long as 24 hours. By comparison, latex paints on drying lose water by evaporation and penetration, and the resin particles fuse together at room temperature to form a continuous film. This may require only a few minutes.

Two typical formulations for styrene-based latex paints are given in Vol. 9, p. 802. It must be emphasized there are an infinite number of possible paint formulations and modifications. Very small changes in the amounts of only one component of a paint may radically change its properties.

The second major use of styrene-based latexes is as an adhesive for coatings for paper and, to a lesser extent, textiles. Like latexes for latex-based paints, these materials contain 50–75% styrene. The paper industry consumes large quantities of synthetic latexes, predominantly various modifications of the styrene-butadiene type. See also *Paper coatings (inorganic)* (Vol. 9, p. 847).

The properties (14,16) of styrene-butadiene latex which make them ideal for paper coating applications include: (1) general upgrading of all coatings in which they are included, (2) smoother printing surface, (3) better fold, (4) excellent varnish holdout, (5) good wet rub resistance for offset work, and (6) reduction of curl. These latexes have become a standard binder. They are used with casein, starch, isolated soybean protein, soybean flour, and glue to produce clay-coated papers, such as book papers, offset papers, high-quality conversion coating base stock, and label and packaging base papers, requiring good lacquer and varnish holdout. In addition, they are used in the manufacture of clay-coated paperboard, wallpaper, fancy coated papers, and decorative wallboard. Precautions should be observed when formulating coating colors with these latexes. Since latex particles carry a negative charge, they are precipitated by polyvalent metal ions usually present in pigments, such as calcium, magnesium, and aluminum. This may be avoided through addition of a complex phosphate such as sodium tetraphosphate. Usually not more than 0.2% is required.

All types of conventional coating equipment may be used for the application of styrene-butadiene latexes. Usually coating operations are carried out on off-machine coating equipment, such as brush coaters, roll coaters, and air knife coaters at speeds of 150–170 ft. per minute. These latexes can also be used on the size press. When used with starch and clay combinations, the latex forms materials that can be processed better than straight starch coatings. Supercalendering the sheet yields better smoothness, which allows better reproduction when printed.

Other applications where these latexes have been used include fabric wall covering where the latex provides abrasion and water resistance, coatings for jute felts in the automobile industry, pigment printing of textiles to improve crock resistance (resistance to rub off), and as a sealer coat between the asphalt-impregnated base and the wear surface in floor coverings and linoleum.

#### NON-FILM-FORMING LATEXES

Non-film-forming styrene-butadiene (over 70% styrene) and pure polystyrene latexes have not found the extensive use of the film-forming types. Pure polystyrene or high-styrene-butadiene latexes are compatible with many other latexes and emulsions and are useful as modifiers for these materials where unusual hardness, strength, and thermoplasticity are desired. The properties of these modified latexes are controlled by varying the quantities of non-film-forming latexes employed with the basic latex. Pure polystyrene and copolymer latexes have also been used to impregnate

and reinforce materials, such as natural and synthetic fibers, provided that sufficient heat can be applied (160°C.) to fuse the polymer and bond the fibers. Materials so treated have the low water absorption, high strength, and good chemical resistance characteristic of polystyrene.

### Styrene-Based Resins

With the large quantities of styrene available after World War II, much work was done to develop new uses for the material. A portion of this work resulted in the development of styrenated drying oils and alkyds useful as improved protective coatings. This work also resulted in styrene-polyester liquid resins designed for laminating and molding large parts. It was found that polystyrene could not be directly combined with drying oils and alkyds and still obtain homogeneous products of desirable properties. This led to blending styrene monomer with drying oils and alkyds and polymerizing the entire mix. Styrene is usually the minority component, but the inherent properties of the polystyrene resulting in the polymerized mixture are responsible for many of the improved properties characteristic of these resins.

#### STYRENE-POLYESTER RESINS

Recently resins produced from styrene and polyesters have become commercially available for use in laminating and potting applications. These resins consist of an unsaturated polyester (alkyd) dissolved in monomeric styrene which upon exposure to heat with or without the presence of catalysts polymerizes to form solid thermoset materials. Monomers, such as diallyl phthalate, triallyl cyanurate, or vinyltoluene, may replace styrene in these reactions. Typical unsaturated alkyds are a result of the reaction of varying proportions of aromatic or aliphatic dibasic acids, such as phthalic, maleic, adipic, or sebacic acid, and propylene or other glycols. See also *Alkyd resins*.

Commercial polyester resins are generally prepared by adding styrene inhibited with *p*-tert-butylpyrocatechol to the base alkyd after esterification is completed and while it is still hot. Once the styrene has been added, the mass is immediately and rapidly cooled to room temperature to avoid polymerization of the mass to a thermoset material in the reaction vessel. Styrene is used in amounts ranging from 20 to 50% by weight.

Commercial polyester resins of this type are supplied in the liquid state, are 100% reactive (solidify without evolution of volatiles), require only contact pressure during cure, and may be used to fabricate large complex objects with or without matched lightweight metal molds. When these resins are solidified and cured, they exhibit toughness, chemical resistance to dilute acids and very weak bases, and good physical properties. In general, the properties of cured resins are a function of (1) the degree of unsaturation present in the polyester, (2) molecular weight of the polyester, and (3) ratio of styrene to polyester.

During curing or polymerization of styrene with polyesters, two primary reactions take place: (1) copolymerization of styrene with polyester, and (2) polymerization of styrene. Reaction (1) is probably dominant initially, but as the concentration of the components changes owing to removal of one or the other during polymerization, the ratio of styrene to polyester will determine which reaction predominates.

The rate of cure of liquid styrene-polyester resins is a function of temperature and may be accelerated through the use of catalysts. One to three percent organic per-

oxide catalysts, such as benzoyl peroxide, are usually used. In addition, certain activators, such as cobalt naphthenate and diethylaniline, are used to increase the rate of solidification by increasing the rate of catalyst activation at the beginning of the reaction. To obtain optimum curing time when very low curing temperatures are used, this is often necessary. Catalysts are available, in cream, paste, or liquid form, which readily dissolve in the liquid resins. Heat is usually applied with hot air ovens, infrared lamps, or high-frequency electronic heating devices, all producing curing temperatures from 60 to 120°C. In some applications curing is accomplished at room temperature.

The rate of cure is increased with increased temperatures, catalyst, and activator concentrations. The reaction is exothermic and the heat evolved ("exotherm") must be controlled. The exotherm is often utilized to supply heat required to carry out the curing process. The exotherm may be controlled by varying the amount of catalyst used and the externally applied temperature of cure. Care must be taken to prevent the exotherm from becoming excessive, for this causes rapid gelation, resulting in rapid shrinkage and subsequent cracking of the finished part. Undesirable low molecular products may also be formed which reduce the strength of the part.

It is possible to obtain cured resins with a wide variety of properties ranging from very rigid to very soft. Rigid resins are generally obtained by employing higher proportions of aromatic dibasic acids and/or increasing the amount of unsaturated component. The type and amount of dibasic acid used exerts the most effect on the properties of the cured resins; however, varying the styrene content will also affect their properties.

The largest use of these resins is the lamination (*q.v.*) of paper, glass mats, and fiber of various types. Lamination may be accomplished by alternating layers of liquid resin and mat, curing under moderate or contact pressure at from room temperature to 120°C. in molds made of filled resinous materials, wood, plaster, or lightweight metals. The forms are generally coated with a lubricant to facilitate release of the finished part from the form. Electrical parts may be successfully potted in styrene-polyester resins. Potted electrical parts exhibit good resistance to temperature changes, water penetration, and mechanical shock.

Styrene-polyester resins have also found use in the fabrication of automobile bodies, glass fiber laminated boat hulls, calking compounds, flat and corrugated sheet, radomes, furniture, and pipe, to mention a few. It should be emphasized there is a tremendous number of formulations making possible suitable resins for specific purposes. This factor plays a prominent role since many styrene-polyesters are developed and produced for specific uses. Two major problems are currently limiting the use of styrene-polyester resins: (1) difficulty in wetting the glass fibers with the liquid resin, and (2) lack of economical mass production fabrication techniques. Solution of these problems would not only open new fields of application for polyesters but would also greatly reduce the cost of items now produced from them.

#### STYRENATED OILS AND ALKYDS

The ready availability of styrene, its chemical nature, and its price stability have led to extensive investigation of the use of styrene in styrenated oils and alkyds for use in the protective coatings field. Many of the inherent properties of polymeric styrene are highly desirable in protective coatings. Some of these properties which have appeared most attractive to the paint and varnish formulators are good color,



hardness, resistance to alkali and water, nonyellowing, and weathering durability. By combining styrene with drying oils, products are formed which possess many of the desirable properties of both basic materials. For example, in styrenated oils the flexibility and adhesion of the natural oils are combined with a good measure of the durability, color retention, and chemical resistance of polystyrene. The oils when styrenated are upgraded by increased solution viscosity and film hardness, and decreased drying time. In general, the properties of styrenated oils resemble those of long oil alkyds. Styrenated oils by virtue of their properties described above are suitable paint vehicles for both architectural and industrial finishes, such as trim paints, gloss enamels, metal primers, and toy enamels.

One of the basic problems encountered when styrene is combined with drying oils is obtaining compatible products. Polystyrene is not soluble in drying oils and cannot be used. Useful homogeneous products can be obtained, however, by polymerizing styrene monomer with drying oils under specified and controlled conditions. The reactivity of the oil, the kind and quantity of the catalyst, the reaction temperature, the ratio of styrene to oil, and the method of monomer addition are important factors which determine the nature of the reaction and the properties of the resulting product.

Styrene reacts with most of the important drying oils to form useful products. Dehydrogenated castor oil is the most suitable. Organic peroxide catalysts are normally used in concentrations of one to three percent by weight based on styrene content. High-temperature peroxides such as di-*tert*-butyl peroxide or *tert*-butyl hydroperoxide are preferred. Polymerization temperatures near the boiling point of the reactant are preferred because improved compatibility and increased reaction rates are obtained. A wide range of styrene to oil proportions may be used, with the best film properties obtained when thirty percent to fifty percent styrene is used.

Styrenated alkyds in many respects exhibit improved properties over styrenated oils and have enjoyed a greater acceptance in the coatings field. Styrenated alkyds generally have better durability, greater chemical resistance, toughness, and adhesion. They dry very rapidly without loss of flexibility. These properties together with high gloss and excellent color retention have made them suitable vehicles for many applications, such as household and industrial finishes and paper coatings. Their limited resistance to hydrocarbons and tendency to mar have restricted their use in automobile finishes.

Styrenated alkyds are obtained by reacting styrene with drying oils or their acids with polyhydric alcohols and polybasic acids. This interaction involves basically two types of reactions: esterification and copolymerization. The technology of the esterification in the preparation of alkyd resins has been developed and may be generally applied to the preparation of styrenated alkyds. The introduction of styrene into an oil-modified alkyd is based on the copolymerization of styrene monomers and the drying oil component. In comparing conventional alkyds with styrenated alkyds the styrene may be viewed as replacing glyceryl phthalate. Therefore, an appraisal of the formulation and properties of styrenated alkyds must consider the presence of styrene; for example, the durability cannot be determined solely on the basis of phthalic anhydride content, but is a function of both the styrene and phthalic anhydride content.

The choice of drying oil or blend of oils employed in preparing styrenated alkyds, as with styrenated oils, is an important factor in successful formulating. The rate of the styrenation reaction and the clarity of the product are influenced by the kind and

amount of unsaturation present in the oil. For example, soybean oil and linseed oil tend to react more slowly with styrene than dehydrated castor oil and chinawood oil.

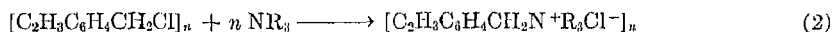
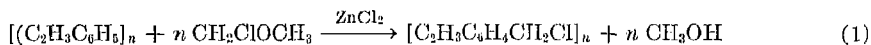
The use of styrene-modified oils and alkyds is restricted to some extent by two factors: (1) limited compatibility with many of the important drying oils or other vehicle additives, and (2) limited solubility in solvents of low Kauri-butanol value. The recent availability of vinyltoluene will remove these limitations when it is used to replace styrene and will upgrade all modified oils and alkyds used in protective coatings.

#### ION-EXCHANGE RESINS

Large quantities of styrene are consumed annually in the production of anion- and cation-exchange resins. See *Ion exchange*.

The most common styrene-based cation-exchange resin is the result of complete sulfonation of styrene-divinylbenzene copolymers. This sulfonation can be carried out in a number of ways to give ion-exchange resin of controllable characteristics. The presence of divinylbenzene serves to crosslink the polymer and render it insoluble but capable of swelling in water. As the divinylbenzene content is increased, the capacity, selectivity, and strength of the ion-exchange beads increase, while their ability to swell and their reactivity decrease.

More recently anion-exchange resins have been developed by subjecting styrene-divinylbenzene copolymer beads to successive reactions of chloromethylation (1) and amination (2). These resins are usually classified as slightly or highly basic anion exchange resins, depending on the type of amine or ammonium group employed. Highly basic ion-exchange resins contain quaternary ammonium groups, whereas slightly basic resins contain primary, secondary, and tertiary amine groups.



The number of exchange groups per styrene unit must be closely controlled since they determine the exchange capacity of the material, the rate of exchange, the density, chemical stability, and physical stability. The advantages of the resins over previously used materials may be summarized as follows: (1) more chemically stable; (2) ease of obtaining spherical beads through suspension polymerization; (3) inexpensive in the case of cation-exchange resins; (4) high exchange capacity per unit volume; (5) flexibility (styrene-divinylbenzene ratio may be varied to obtain desired properties).

These resins are used in granular form usually having a mesh size from 20 to 50. They may be prepared as beads or ground to granules of the desired size. Regeneration consists of a water backwash to remove filtered solids from the column, followed by passing through the column a strong solution of a compound producing the ion to be regenerated in the resin. Cation resins are regenerated with strong acids, and anion resins with brine. Recent systems mix both anion- and cation-exchange resins together in the same column when removal of both cations and anions is desired. When saturated, both resins are regenerated within the column in the same manner as when they are employed separately. Continuous ion exchange systems eliminate the need for shutdown for regeneration.

## Bibliography

- (1) Alfrey, T., Jr., Bohrer, J. J., and Mark, H., *Copolymerization*, Interscience, New York-London, 1952.
- (2) A.S.T.M., *Standards on Plastics*, March 1953, pp. 534-8.
- (3) Bamford, C. H., and Dewar, M. J., *Nature*, **157**, 845 (1946); *Proc. Roy. Soc. (London)*, **192**, 309 (1947).
- (4) Boundy, R. H., and Boyer, R. F., *Styrene, Its Polymers, Copolymers, and Derivatives*, Reinhold, New York, 1952. Table XI and Figs. 3, 5, 6, and 10 courtesy Reinhold Publishing Corp.
- (5) Burnett, G. M., and Melville, H. W., *Trans. Faraday Soc.*, **46**, 772 (1950).
- (6) DeBell, J. M., Goggin, W. C., and Gloer, W. E., *German Plastics Practice*, DeBell and Richardson, Inc., 1946.
- (7) Dow Chemical Co., Tech. Bull., "Styron 647."
- (8) Dow Chemical Co., Tech. Bull., "The Crazing of Polystyrene."
- (9) Melville, H. W., and Valentine, L., *Trans. Faraday Soc.*, **46**, 210 (1950).
- (10) *Modern Plastics Encyclopedia*, Plastics Properties Chart, Plastics Catalog Corp., N.Y., 1953.
- (11) Payne, H. F., *Paint, Oil, Chem. Rev.* (Oct. 22, 1953).
- (12) Peterson, N. R., Henson, W. A., *Off. Dig. Federation Paint & Varnish Production Clubs* (Aug. 1952).
- (13) Samaras, N. N. T., Perry, E., *J. Appl. Chem. (London)*, **1**, 243 (1951).
- (14) Silvernail, L. H., and Heiser, E. J., *Tappi*, **36** [10] (Oct. 1953).
- (15) Smith, V. W., *J. Am. Chem. Soc.*, **70**, 3695 (1948); **71**, 4077 (1949).
- (16) The Paper Industry, "Styrene-Butadiene Type Latex Upgrades Paper Coatings," March 1953.
- (17) Alfrey, T., Jr., *Mechanical Behavior of High Polymers*, Interscience, New York-London, 1948.
- (18) Bovey, F. A., and Kolthoff, I. M., *J. Polymer Sci.*, **5**, 487, 569, 748 (1950); *J. Am. Chem. Soc.*, **70**, 791 (1948).
- (19) Dunlop, R. D., and Reise, F. E., *Ind. Eng. Chem.*, **40**, 654 (1950).
- (20) Elly, J., Haward, R. N., and Simpson, W., *J. Appl. Chem. (London)*, **1**, 347 (1951).
- (21) Harkins, W. O., *J. Am. Chem. Soc.*, **69**, 1428 (1947).
- (22) Hohenstein, W. P., *Polymer Bull.*, **1**, [1], 13 (1945).
- (23) Smith, W. V., and Ewart, R. H., *J. Chem. Phys.*, **16**, 592 (1948).
- (24) U.S. Pat. 2,108,044 (1938), J. W. C. Crawford and J. McGrath.
- (25) U.S. Pat. 2,287,188 (1942), L. A. Matheson and R. F. Boyer (to Dow Chemical Co.).
- (26) U.S. Pat. 2,530,409 (1950), K. E. Stuber and J. L. Amos.

J. A. STRUTHERS, R. F. BOYER, AND W. C. GOGGIN

**SUBERIC ACID**,  $\text{HOOC}(\text{CH}_2)_6\text{COOH}$ . See *Acids, dicarboxylic*, Vol. **1**, p. 154.

**SUBSTANTIVE DYES**. See *Azo dyes*, Vol. **2**, p. 244.

**SUBTILIN**. See *Antibiotics*, Vol. **2**, pp. 16, 26, 31.

**SUCCINALDEHYDE**,  $(\text{CH}_2\text{CHO})_2$ . See *Aldehydes*, Vol. **1**, p. 336; *Succinic acid*.

**SUCCINCHLORIMIDE**,  $\text{CO.CH}_2\text{CH}_2\text{CO.NCl}$ . See *Chloramines and chloroamines*,

Vol. **3**, p. 673; *Succinic acid*.

## SUCCINIC ACID AND SUCCINIC ANHYDRIDE

Succinic acid,  $\text{HOOCCH}_2\text{CH}_2\text{COOH}$ , formula weight 118, occurs widely in nature in both plant and animal matter (3). The acid and its anhydride have many unique properties, the most interesting of which is the reactivity of the methylene groups. As in unsaturated maleic or fumaric acid (see Vol. 8, p. 680), from which it may be derived, each group can be caused to react in some manner under suitable experimental conditions, so that it has been used advantageously as an intermediate in the synthesis of a wide variety of complex organic compounds.

Succinic acid is classed at present as one of our important intermediates in the manufacture of pharmaceuticals. It is also a valuable ingredient in the synthesis of plastics, elastomers, protective coatings, electrical insulation, and many other industrial products.

The acid was first obtained by Agricola in 1550 by distilling amber, from which it can be obtained in 3–8% quantities. Part of the acid is present as esters of other constituents. It is also found in some varieties of lignite, in resins, in turpentine oils and in animal fluids. It is formed in both the chemical and biochemical oxidation of fats, in the fermentation of calcium malate or ammonium tartrate, and in the alcoholic fermentation (*q.v.*) of sugar. Its presence in both plant and animal matter has led to extensive phytochemical and zoochemical studies, especially those directed toward its role in various metabolisms and other vital processes (3).

## Physical and Chemical Properties

The acid occurs both as colorless triclinic and as monoclinic prisms, which dissolve in water, alcohol, diethyl ether (3), anhydrous glycerol, acetone, and various aqueous mixtures of the last two solvents. The monoclinic crystals are triboluminescent. When heated below its melting point under reduced pressure, for example

TABLE I. Physical Properties.

Property	Succinic acid	Succinic anhydride
M.p., °C.	181–185	119–120
B.p., °C.	(Dehydrates at 235°C.)	261
Sublimation point, °C., 1–3 mm.	132–152	90
Sp.gr.	1.552–1.577	1.572
Solubility, g./100 g. soln.		
Water at 0°C.	2.88	—
Water at 100°C.	121	—
96% alcohol at 15°C.	9.99	—
Ether at 15°C.	1.25	—
Dissociation constant		
$K_1 \times 10^{-3}$	6.52–6.65	—
$K_2 \times 10^{-6}$	2.3	—
Average sp. heat, cal./g., (0–35°C.)	0.2965	—
Heat of combustion, kg.-cal./mole	356.2–357.4	369.9–373.1
Heat of solution in 60 parts of water, cal./mole	6528	—
Dipole moment at 20°C., e.s.u. $\times 10^{-18}$	—	4.20
Magnetic susceptibility, e.s.u.	–57.47	–43.85
Dielectric constant, 5 kilocycles (3–97°C.)	2.29–2.90	—

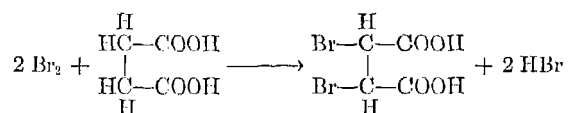
160–65°C. and 2.5–5 mm. Hg, the acid sublimes. It is readily adsorbed from solution by charcoal. See also Table I (3,12,18,21,22).

The anhydride occurs as rhombic pyramidal or bipyramidal crystals. Unlike those of the acid, these crystals are relatively insoluble in both water and ether, but they are soluble in alcohol. See also Table I.

#### CHEMICAL PROPERTIES

Succinic acid undergoes most of the reactions characteristic of dicarboxylic acids. A common characteristic of succinic acid and its derivatives is the *succinoyl grouping*,  $-(O:)C-CH_2-CH_2-C(:O)-$ . This grouping, consisting of two adjacent methylene groups flanked by the two symmetrically attached unsaturated carbonyls, is largely responsible for the reactivity of the methylene groups. See also *Acids, dicarboxylic*.

**Halogenation.** The reactivity of the methylene groups is shown in the reactions of succinic acid and its anhydride with halogens. Succinic acid itself does not react with bromine in an open vessel but does give almost quantitative yields of *meso*-dibromosuccinic acid when heated at 100°C. in a sealed tube (3). The reaction is complete within two to four days and takes place both in the presence and absence of water:



There is no evidence that either the *dl*-acid or the monobromo acid is formed. If either were produced as an intermediate, it would probably be rapidly converted to the *meso*-dibromo acid under the conditions employed. When more than an equivalent amount of water is present, brominated hydrocarbons are produced which reduce the yield of the dibromo acid.

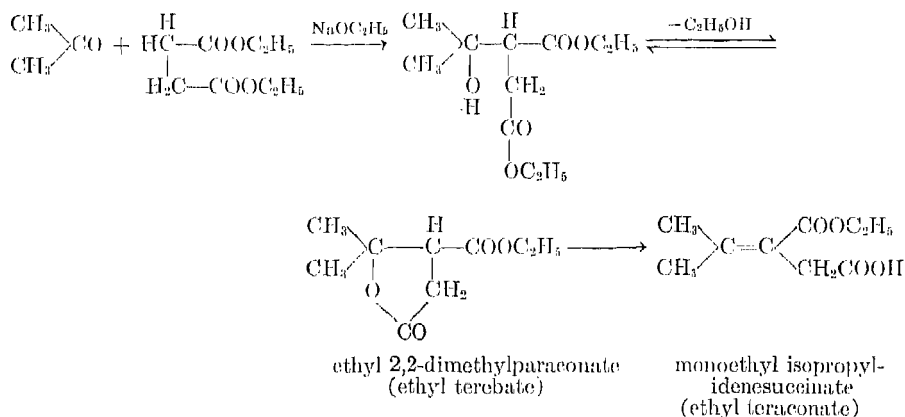
The anhydride, when heated with a molecular equivalent of bromine, gives principally the monobromo derivative, b.p. 130–33°C. With two moles of bromine it yields the *dl*-2,3-dibromosuccinic anhydride, m.p. 118–19°C.

Diethyl succinate when treated with an excess of chlorine in sunlight is completely chlorinated, yielding small needles of *bis*(pentachloroethyl) tetrachlorosuccinate,  $\text{Cl}_3\text{C}-\text{CCl}_2\text{OCCCCl}_2\text{CCl}_2\text{COOCCl}_2\text{CCl}_3$ .

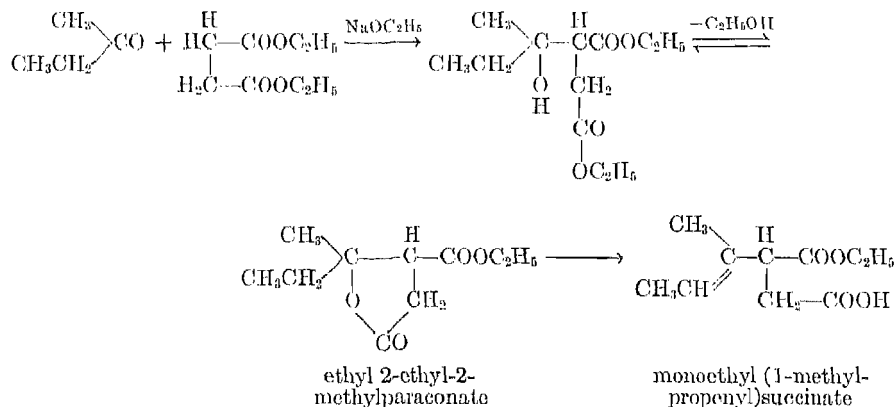
Succinic acid reacts with an equal molecular amount of phosphorus pentachloride at 120–130°C. to yield succinoyl chloride.

**Condensations with Ketones and Aldehydes.** One of the most interesting reactions of the succinoyl grouping is shown in the condensation of succinic diesters with aldehydes and ketones in the presence of sodium alkoxides. Unlike other compounds with reactive methylene groups, succinates do not form  $\beta$ -diketones (see Vol. 8, p. 146) by a Claisen type of reaction except in specific instances where polyketones are produced as by-products in small amounts. Instead, half-esters of alkylidenesuccinic acids are usually the major products. These are formed by the *Stobbe condensation* (14) which is peculiar to succinic esters and substituted succinic esters. From available evidence, the Stobbe reaction takes place in three steps: the reactants first form an aldol or a ketol that loses alcohol to give a  $\gamma$ -lactone ester known as a *paraconate*,

which in turn rearranges to the *alkylidenesuccinic acid half-ester*. A typical Stobbe condensation is that of acetone and diethyl succinate:

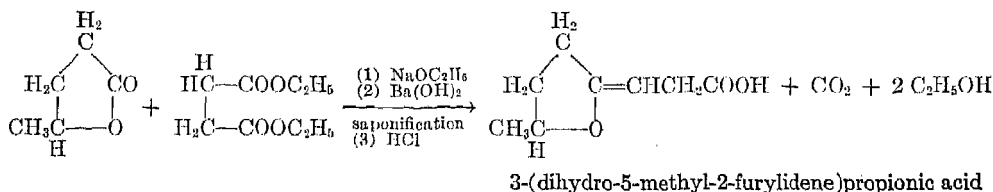


Isomers of the alkylidenesuccinates are also obtained in varying amounts, depending upon the experimental environment and the structure of the ketone. *Alkenylsuccinic half-esters*, for example, are likely to be the predominating products when the ketone contains a methylene group, as with methyl ethyl ketone:

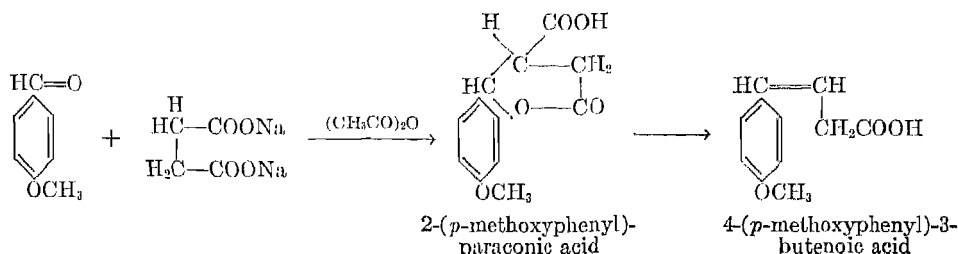


A small amount of the (1-methylpropylidene)succinate is also formed in this reaction.

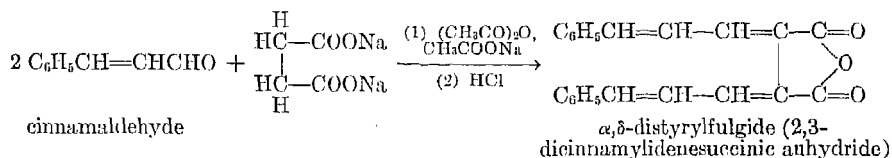
Decarboxylated products are obtained when the reaction is carried out at elevated temperatures. These can be formed from either the intermediate paraconates or from the alkylidenesuccinates (substituted itaconates), since both types of compounds lose carbon dioxide quite easily (15). Such a reaction occurs with 4-hydroxyvaleric acid  $\gamma$ -lactone:



A similar loss of carbon dioxide occurs in the reaction of anisaldehyde with disodium succinate and acetic anhydride (13):

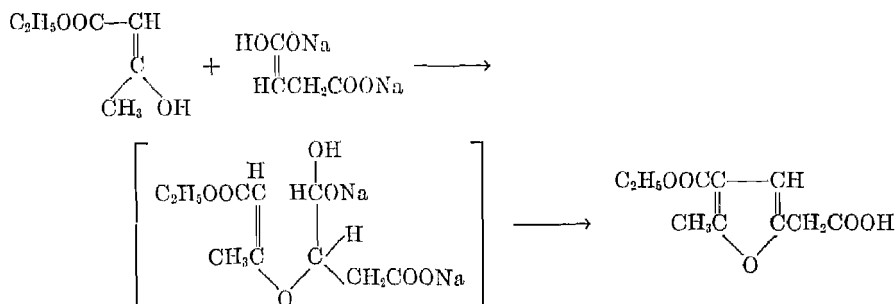


*Dialkylidenesuccinic acids and anhydrides* may be formed in a similar manner from a number of aromatic aldehydes:

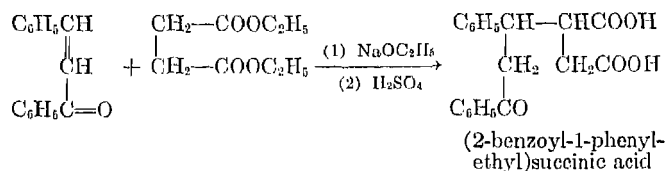


These highly unsaturated anhydrides are known as *fulgides*. They are intensely colored. Small amounts of 6-phenyl-3,5-hexadienoic acid,  $\text{C}_6\text{H}_5\text{CH=CHCH=CH-CH}_2\text{COOH}$ , and 1,8-diphenyl-1,3,5,7-octatetraene,  $\text{C}_6\text{H}_5\text{CH=CHCH=CHCH=CH-CH=CHC}_6\text{H}_5$ , are formed also. The yield of the latter can be increased to 33% of the theoretical amount when lead oxide (lead acetate) is substituted for sodium acetate in the reaction. Dilactones are most likely formed during these preparations, giving the observed products. *Half-esters of dialkylidenesuccinic acids* may be prepared by allowing the diester of an alkylidenesuccinic acid to react with a molecular equivalent of the aldehyde by the Stobbe reaction.

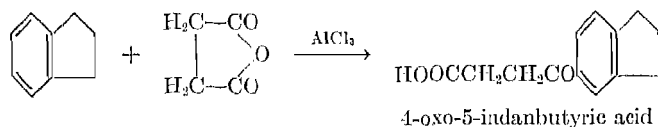
The Stobbe condensation is probably the most characteristic reaction of succinic acid esters. This is evident from the fact that only a very few failures are reported (14), and these can generally be attributed to steric hindrance. The  $\beta$ -keto esters, like ethyl acetoacetate (see Vol. 5, p. 845) and certain unsaturated ketones (*q.v.*), such as chalcone, react in a different manner. The former yields derivatives of furan-acetic acid, possibly through the union of both reactants in their enol forms:



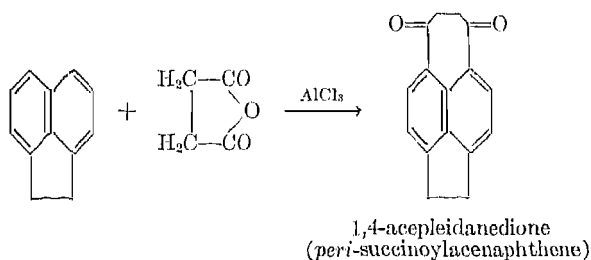
The reaction at best is rather complex since carbon dioxide, ethyl acetate, and acetone are also formed as by-products. Direct addition instead of condensation occurs in the case of chalcones:



**Friedel-Craft Reactions.** Like other dibasic anhydrides, succinic anhydride readily undergoes addition to aromatic compounds in the presence of anhydrous aluminum chloride (this type of reaction is known as *succinolation*) to form various derivatives of 4-oxobutyric acid (4), as for example in the reaction with indan:

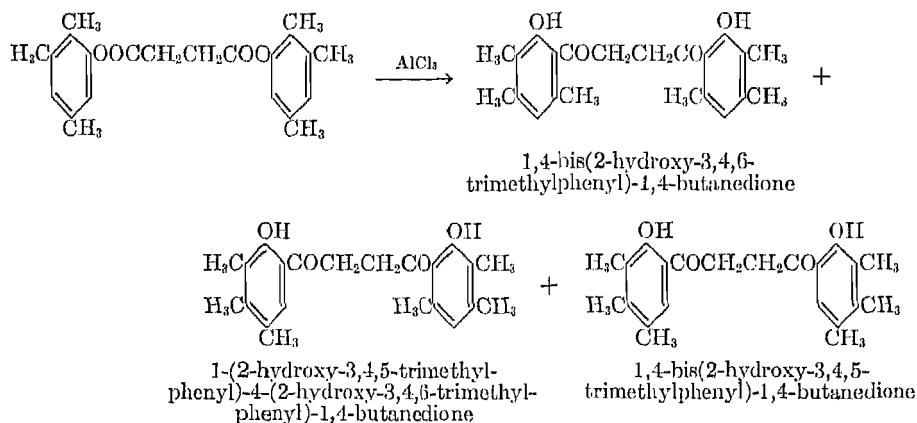


With acenaphthene, both carbonyl groups become attached to the hydrocarbon (2):



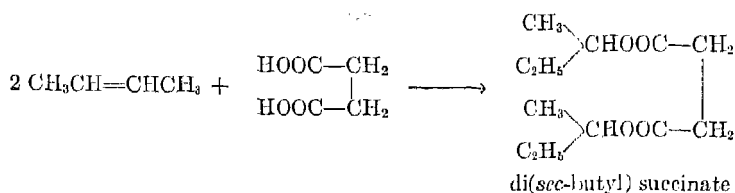
This product contains an unusual seven-membered diketo ring.

An interesting rearrangement (Fries rearrangement) also takes in the presence of aluminum chloride (23) with certain aromatic succinates, such as bis (2,3,5-trimethylphenyl) succinate:

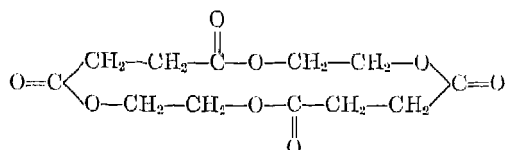


**Esterification.** Succinic acid and its anhydride are readily esterified by the usual methods. One interesting procedure employs an unsaturated hydrocarbon for this purpose (26), to yield the secondary esters:



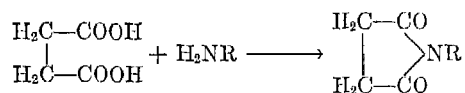


The polyesters of the various glycols can be depolymerized in the presence of stannous chloride to yield interesting poly-membered ring products (7). Poly(ethylene succinate), for example, gives the 16-membered cyclic dimer of ethylene succinate, 1,4,9,12-tetraoxacyclohexadecane-5,8,13,16-tetrane:

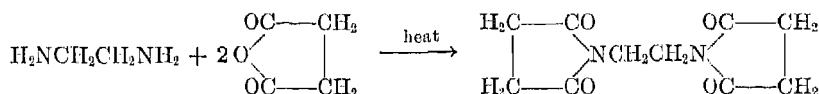


Poly(propylene succinate) yields both a cyclic monomer and cyclic dimer.

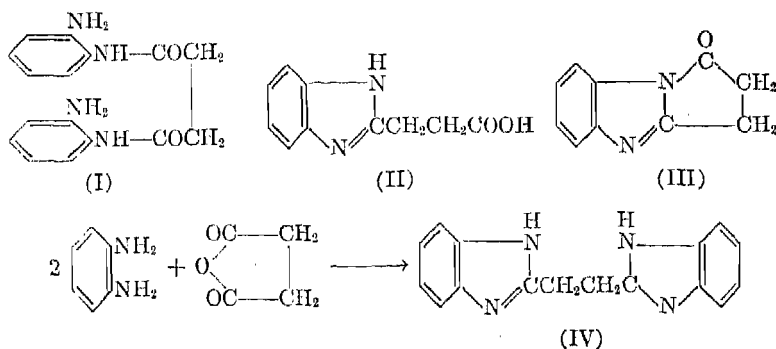
**Reactions with Amino Compounds.** Several useful reactions also occur with compounds containing an amino group; in no case do they involve the methylene groups of succinic acid or its derivatives. Included is the reaction of succinic acid with ammonia and amines at elevated temperatures to give the various *succinimides* (R = hydrogen, alkyl, or aryl):



Diamines such as ethylenediamine or *m*-phenylenediamine react with two moles of succinic anhydride to yield *N,N'*-disuccinimides:

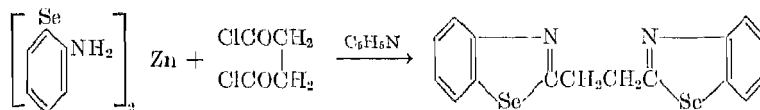


By contrast, *o*-phenylenediamine, in equimolecular proportion with succinic anhydride, gives a mixture of *o,o'*-diaminosuccinanilide (I) and 2-benzimidazolepropionic acid (II), while two moles of the diamine yield 1,2-di-2-benzimidazolyethane (2,2'-ethylene-bisbenzimidazole) (IV):

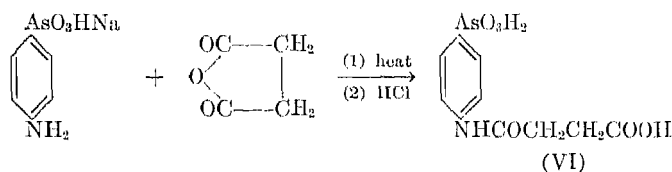
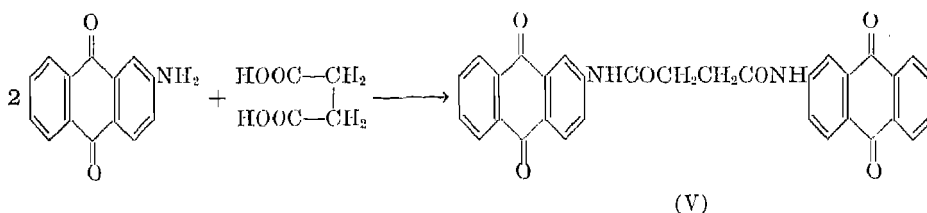


2-Benzimidazolepropionic acid (II), when heated at 230–40°C., yields  $\alpha$ -oxo-1,2-propylenebenzimidazole (2,3-dihydropyrrolo[1.2-*a*]benzimidazol-1-one) (III) through further cyclization and loss of a mole of water.

The zinc salt of *o*-aminoselenophenol when treated with succinoyl chloride in pyridine gives 1,2-di-2-benzoselenazolyethane (2,2'-ethylenebisbenzoselenazole):

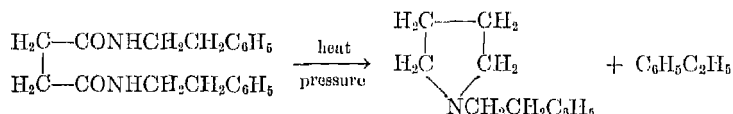


The formation of mono- and diamides (succinamic acids and succinamides) by the usual procedures with various amines has been extensively used in the synthesis of dyes, insecticides, and medicinals, for example, the preparation of *N,N'*-di-2-anthraquinonylsuccinamide (V) from 2-aminoanthroquinone and of *N-p*-arsonosuccinanilic acid (VI) from atoxyl (sodium hydrogen arsenilate):

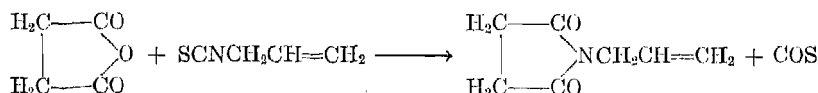


Benzamide, when heated with a molecular equivalent of succinic anhydride in benzene, yields a mixture of *N,N'*-dibenzoylsuccinamide and *N*-benzoylsuccinamic acid.

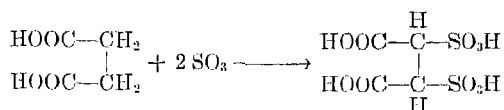
When various *N*-substituted succinamides are heated in dioxane at 250°C. under a hydrogen pressure of 200–300 atm. over a copper–chromium oxide catalyst, fair yields of the respective pyrrolidines are obtained. *N,N'*-Bis(2-phenylethyl)succinamide, for example, yields 65% of *N*-(2-phenylethyl)pyrrolidine and 13% of ethylbenzene:



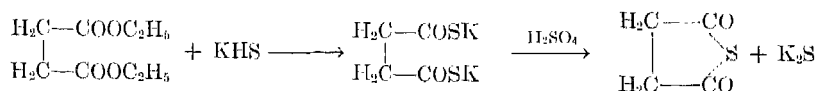
**Reactions with Sulfur Compounds.** Allyl mustard oil (allyl isothiocyanate) reacts with succinic anhydride to give *N*-allylsuccinimide by splitting off carbonyl sulfide:



Sulfur trioxide gives 2,3-disulfosuccinic acid as the result of its reaction with both methylene groups of succinic acid:



Potassium hydrogen sulfide reacts with diethyl succinate to produce dipotassium dithiosuccinate, which, when treated with sulfuric acid, yields dihydro-2,5-thiophenedione (dithiolsuccinic anhydrosulfide):



**Oxidation.** Hydrogen peroxide under various experimental conditions can be induced to yield either peroxysuccinic acid,  $(\text{CH}_2\text{COOOH})_2$ , 2,2-dihydroxysuccinic acid, malonic acid, or a mixture of acetaldehyde, malonic and malic acids. Potassium permanganate gives either oxalic acid or a mixture of malic and tartaric acids. Sodium perchlorate can be employed to obtain 3-hydroxypropionic acid.

**Degradation Reactions.** Heated under various conditions, succinic acid or its salts yield  $\gamma$ -ketopimelic dilactone (4,4-dihydroxyheptanedioic acid  $\gamma,\gamma$ -dilactone),  $\text{OC}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{C}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}$ ; 1,4-cyclohexanedione; ethane; a mixture of propionic

acid, acetic acid, acrylic acid, and acrolein; oxalic acid; heptadiene; or cyclopentanone and furan. In the presence of zinc at 350–400°C. succinic acid gives high-melting hydrocarbons, and when subjected to electrolysis, ethylene and acetylene.

### Manufacture

Succinic acid is generally produced by the **hydrogenation** of maleic anhydride or fumaric acid (see Vol. 8, p. 689) and is isolated either as the free acid or as the anhydride. Several different processes are available for this purpose. All of them give excellent commercial yields. They include, for example, treating an aqueous solution of sodium maleate with hydrogen gas at 100°C. under 2500 p.s.i. pressure in the presence of a Raney-nickel catalyst; reduction with hydrogen at room temperatures with colloidal palladium as catalyst; electrolytic reduction; and reduction with sulfuric acid and zinc. The acid may also be produced by hydrolyzing succinonitrile with either aqueous alkali or acid (see Vol. 9, p. 356). Numerous other methods have also been employed.

**Oxidation Methods.** Various quantities of succinic acid are obtained when spermaceti and other waxes (*q.v.*), butanediol, butyric acid, sebacic acid, stearic acid, methyleyclopentane, tetrahydrofuran, and 3-formylpropionic acid are treated with nitric acid. Small amounts are formed when cyclohexane is oxidized for the production of adipic acid (Vol. 1, p. 153). Other oxidation methods include treating glutamic acid or butyrates with hydrogen peroxide, or acetic acid with potassium peroxysulfate,  $\text{K}_2\text{S}_2\text{O}_8$ , or acetyl peroxide. The last method is the one that can be used for preparing tetrachloro- and tetrafluorosuccinic acids from dihaloacetic acids. Furfural has been oxidized to succinic anhydride with Caro's acid,  $\text{H}_2\text{SO}_5$ . The vapor-phase oxidations of petroleum wax and of butyrolactone have also been recommended. These methods use a vanadium oxide or copper oxide catalyst and yield a mixture of both the acid and the anhydride. Electrolytic oxidations have been employed with ethyl potassium malonate, tetrahydrofurfuryl alcohol, and tetrahydrofuran.

**Fusion Methods.** These include the treatment of milk sugar (lactose), gum arabic, or cinnamic acid with hydrated lime; cellulosic materials, such as corn cobs, with caustic alkali (41); and pyrrole (*q.v.*) with caustic and hydroxylamine. This last method first gives an oxime, which may then be converted to the acid.

**Condensation Reactions.** Various products may be treated with potassium cyanide and then hydrolyzed to give succinic acid. This method includes the use of such compounds as 3-chloro- or 3-iodopropionic acid, ethylene dichloride, salts of acrylic acid,  $\beta$ -propiolactone (hydraacrylic acid  $\beta$ -lactone), and 3-formylacrylic acid (malealdehydic acid). Both the C-13 carboxyl- and the methylene-labeled acids have been prepared from the isotopic dinitriles obtained from the suitable ethylene dibromides.

Succinic acid may also be obtained from the reaction of ethyl cyanoacetate and formaldehyde cyanohydrin, and from the reaction of hydrocyanic acid and ethylene (42).

**Miscellaneous Methods.** Malic and tartaric acids may be reduced with hydriodic acid. Succinic acid may also be prepared by the controlled decarboxylation of ethanetricarboxylic acid and by various fermentation processes.

**Preparation of the Anhydride.** The anhydride has been obtained by the dry distillation of maleic acid, by dehydrating succinic acid at elevated temperatures, and by treating succinic acid with thionyl chloride, phosphorus pentachloride, diketene, succinyl chloride, and acetic anhydride. It may also be prepared by treating the diethyl ester with boron chloride in a closed flask at 250°C.

**Economics.** Very little information is available on the commercial production of succinic acid and its derivatives. The U.S. Tariff Commission Reports show that 244,000 pounds of acid and anhydride were produced in 1942, 24,000 pounds of the acid were sold in 1943, and 29,000 and 60,000 pounds of the acid were produced, respectively, in 1946 and 1947.

**Grades and Containers.** Both succinic acid and succinic anhydride are sold in one grade. The former is known as "succinic acid purified," while the latter is called "succinic anhydride distilled." In bulk quantities both are packed in lined Leverpak fiber drums, 250 lb. net being the standard package for the acid, and 275 lb. for the anhydride. Quality is based upon the solidifying points, color, total acidity, turbidity of a 5% aqueous solution, and freedom from impurities such as maleic acid, maleic anhydride, chlorides, sulfates, and heavy metals.

*N*-Bromosuccinimide containing a minimum of 44.5% active bromine is available in 50-lb. drums, while *N*-chlorosuccinimide with a chlorine content of 25.0% or more is available in similar containers.

Succinoyl chloride is offered in small pilot plant quantities.

### Uses

Succinic acid and its derivatives are used as antispasmodics (27), expectorants and diuretics. They are also employed in the treatment of typhoid, acute exanthema, epilepsy, cramps, hysteria, gout, and rheumatism. The ammonium salts are used internally for control of spasmodic pains, labor pain, uterine contractions, and delirium tremens. The calcium salt of the benzyl ester has been employed in rheumatic fever treatment (11), and sodium succinate as an antidote in heavy-metal and barbiturate poisoning. The di-*n*-butyl ester has been used as a solvent in parenteral injections (10). Other esters have been shown to have Vitamin A, antihemorrhagic, antispas-

modic, and curare-like properties (24,27,29). Cortical hormone esters have been used in various investigations for their important physiological properties (37). 2-[ $\alpha$ -(2-Dimethylaminoethoxy)- $\alpha$ -methylbenzyl]pyridine succinate (doxylamine succinate) has been shown to be an antihistamine (5) (see Vol. 7, p. 471). Succinic acid and its anhydride are also employed in the manufacture of sulfa drugs (*q.v.*) (6), arsenicals, mercurials, such as mercuric succinimide (see Vol. 8, p. 895), and salts of the *S*-gold and *S*-antimony derivatives of mercaptosuccinic acid. They have also been used for preparing other therapeutics (16,36) such as *N*-methyl-2-phenylsuccinimide, which is used as an anticonvulsant (see *Stimulants and depressants*).

Both the Stobbe synthesis and Friedel-Craft reactions (see pp. 183 and 184), have been extensively employed in the synthesis of polynuclear aromatic compounds. Here they are used for the purpose of adding further aromatic rings to the compounds, as in the synthesis of naphthacenes, phenanthrenes, acepleidanes, steroids, and similar complex ring structures. A good example is the synthesis of various *substituted benzanthracenes* reported as having carcinogenic properties which have been of interest in cancer studies (20). The Friedel-Craft reaction with succinic anhydride has also been employed in synthesis of long-chain hydrocarbons, dibasic acids, and 2-alkylbutadienes. The Stobbe synthesis is employed for preparing fulgides which have the interesting property of varying in color upon exposure to light of different intensities.

Succinic acid is used as a photographic chemical, as a standard in preparing volumetric solutions, and as a reagent in the separation of iron from other metal salts. The acid has been recommended also for use in cleaning compounds and for treating the surfaces of aluminum and magnesium alloys before painting. It is used in the manufacture of perfumes and dyes. Amides have been suggested as lathering agents and diquinonyldiamides, such as *N,N'*-di-1-anthraquinonylsuccinamide, as printing assistants (32).

Alkyd resins (*q.v.*) made with large amounts of succinic anhydride have outstanding electrical insulating properties. In combination with other acids (25,28,29,40), they impart flexibility to both the coating and plastic types. Adhesives and plasticizers (33) have been produced from simple esters. The dibenzyl ester has been employed in the dyeing of vinyl yarn (31) (see also *Textile fibers, synthetic*) and the lead salts of the acid have been recommended as stabilizers for vinyl resins (see *Vinyl compounds, resins, and plastics*). The cellulose half-ester has been recommended for use as an acidic cation-exchange material (30). Silicone-alkyds (38), from reaction with silicones, have been prepared and give coatings with a high resistance to deterioration at elevated temperatures.

Succinic acid and succinic anhydride are used in the manufacture of flexible types of polyester resins employed in the production of glass fiber-reinforced plastics.

The 2,4,5-trichlorophenyl ester has been employed for seed treatment. Both dialkyl succinates and the *N,N*-dialkyl derivatives of succinamic acid show unusual promise as repellents for mosquitoes, black flies, and sand flies (2,9).

Alkenylsuccinic anhydrides, prepared commercially by the reaction of maleic anhydride with olefins, have been used in preparing additives for lubricants and anti-rusting compounds for oils.

### Derivatives

There are several derivatives of succinic acid that are sold commercially. Many of these, like dodecenylsuccinic anhydride and dichlorosuccinate, are produced from

maleic anhydride (see Vol. 8, pp. 688, 690). Three of the most common derivatives produced from succinic anhydride are succinimide, *N*-bromosuccinimide, and *N*-chlorosuccinimide.

**Succinimide**, m.p. 125°–26°C., is made by heating a concentrated solution of diammonium succinate until ammonia and water are no longer evolved, then fractionating the molten product and collecting the material that boils at 285–90°C. It is also prepared by heating succinic acid in a stream of ammonia or with urea or formamide, or by treating aqueous acrylonitrile with an alkali cyanide. It is used largely for the preparation of *N*-halogen-substituted succinimides.

***N*-Halosuccinimides** are prepared by first forming a metal salt of the imide before adding the halogen, or by using hypochlorites as the halogenating agents. At elevated temperatures (160°C.), succinimide undergoes chlorination at the methylene groups to yield a mixture of chloro- and 2,3-dichloromaleimide. Heated with a mole of bromine in chloroform at 120°C., it gives 2-bromosuccinimide.

***N*-Bromosuccinimide** has been extensively used as a selective halogenating and oxidizing agent in the synthesis of cortisones and other hormones (*q.v.*; see also *Sterols and steroids*). This product has the unique property of bringing about halogen substitution at methylene groups adjacent to unsaturated bonds without adding to the ethylene group. By varying reaction conditions, it can be used as a reagent for selective substitution, including the substitution of side-chains attached to aromatics; for controlled dehydrogenation; for nuclear addition to aromatic compounds; for the formation of bromohydrins; or for selective oxidation of alcohol groups to ketones or aldehydes. These reactions have been applied to all types of compounds, including olefins, carbonyl compounds, aromatics, heterocyclics, and even saturated substances.

***N*-Chlorosuccinimide** (succinchlorimide, N.F. IX) (see Vol. 3, p. 673), is a powerful germicide and deodorant. It has been used widely as a disinfecting agent and to a limited extent as a halogenating agent similar to *N*-bromosuccinimide.

Another derivative is **succinonitrile**, which is obtained as a by-product in the manufacture of acrylonitrile (*q.v.*) (see also Vol. 9, p. 369). Succinonitrile has been recommended for use as a brightener in nickel-plating baths, and as a selective solvent for extracting aromatic compounds from petroleum distillates.

**Succinaldehyde** (butanedial),  $\text{OHCCH}_2\text{CH}_2\text{CHO}$ , is commercially available in limited quantities as its stable, water-soluble acetal *2,5-dithoxytetrahydrofuran*,  $\text{C}_2\text{H}_5\text{OCH}(\text{CH}_2\text{CH}_2\text{CHOC}_2\text{H}_5)_2$ , formula weight 206.28, b.p. 196°C. at 5 mm. Hg,  $d_{20}^{20}$

1.081.

### Bibliography

- (1) Applewhite, K. H., and Cross, H. F., *J. Econ. Entomol.*, **44**, 19 (1951).
- (2) Baekelheide, V., Langeland, W. E., and Liu, C. T., *J. Am. Chem. Soc.*, **74**, 2432 (1951).
- (3) Beilstein, 4th ed., Vol. II, pp. 601–6; 1st Suppl., pp. 259–62; 2nd Suppl., pp. 542–46; Vol. XVII, p. 407; 1st Suppl., p. 228; 2nd Suppl., p. 429; Vol. XXI, p. 380.
- (4) Berliner, E., *Organic Reactions*, Wiley, N.Y., 1949, Vol. V, pp. 230–89.
- (5) Brown, B. B., and Werner, H. W., *Am. Allergy*, **6**, 122 (1948).
- (6) Calloman, F. T., and Raiziss, G. W., *Pharmacol. J.*, **79**, 200 (1943).
- (7) Carothers, W. H., and Arvin, J. A., *J. Am. Chem. Soc.*, **51**, 2560 (1929).
- (8) De Foliart, G. R., *J. Econ. Entomol.*, **44**, 265 (1951).
- (9) Develotte, J., *Ann. chim.*, [12] **5**, 215 (1950).

- (10) Gross, E. G., *Proc. Soc. Exptl. Biol. Med.*, **56**, 172 (1944).
- (11) Gubner, R., and Szues, M., *New England J. Med.*, **233**, 652 (1945).
- (12) Hill, T. L., *J. Chem. Phys.*, **12**, 56 (1944).
- (13) Johnson, J. R., *Organic Reactions*, Wiley, N.Y., 1942, Vol. I, pp. 211-65.
- (14) Johnson, W. S., and Daub, G. H., *Organic Reactions*, Wiley, N.Y., 1951, Vol. VI, pp. 2-73.
- (15) Johnson, W. S., and Hunt, R. H., *J. Am. Chem. Soc.*, **72**, 935 (1950).
- (16) Katz, L., *J. Am. Chem. Soc.*, **73**, 4009 (1951).
- (17) Kreuchunas, A., *J. Am. Chem. Soc.*, **75**, 3341 (1953).
- (18) Kushner, M., and Weinhouse, S., *J. Am. Chem. Soc.*, **71**, 3558 (1949).
- (19) McNeight, S. A., and Smyth, C. P., *J. Am. Chem. Soc.*, **58**, 1718 (1936).
- (20) Newman, M. S., and Gaertner, R., *J. Am. Chem. Soc.*, **72**, 264 (1950).
- (21) Pinching, G. D., and Bates, R. G., *J. Research Natl. Bur. Standards*, **45**, 444 (1950).
- (22) Singh, B. K., Mahan, K. M. S., Agarwal, S. L., Hog, N., and Singh, M., *Proc. Indian Acad. Sci.*, **A22**, 163 (1945).
- (23) Smith, L. J., and Holmes, R. R., *J. Am. Chem. Soc.*, **73**, 3847 (1951).
- (24) Vanderhaeghe, H., *Nature*, **167**, 527 (1951).
- (25) Yager, W. A., and Baker, W. O., *J. Am. Chem. Soc.*, **64**, 2164 (1942).
- (26) Zavgoradnii, S. V., *Trudy Voronezh. Gosudarst Univ. (Acta Univ. Voronegiensis)*, **10**, No. 2, 41 (1938).
- (27) U.S. Pat. 1,621,757 (March 22, 1927), P. Seydel.
- (28) U.S. Pat. 1,993,028 (March 5, 1935), E. G. Petersen and E. R. Littmann (to Hercules Powder Co.).
- (29) U.S. Pat. 2,218,553 (Nov. 22, 1941), I. Rosenblum.
- (30) U.S. Pat. 2,352,261 (June 27, 1944), G. D. Hiatt and J. Emerson (to Eastman Kodak Co.).
- (31) U.S. Pat. 2,362,376 (Nov. 7, 1944), K. Heymann (to American Viscose Corp.).
- (32) U.S. Pat. 2,371,102 (March 6, 1945), R. H. Kienle and C. A. Amick (to American Cyanamid Co.).
- (33) U.S. Pat. 2,385,377 (Sept. 25, 1945), C. Opp (to Interchemical Corp.).
- (34) U.S. Pat. 2,407,726 (Sept. 17, 1946), L. D. Smith and W. B. Renfrow (to Regents of University of Minnesota).
- (35) U.S. Pat. 2,440,218 (April 20, 1948), F. Bergel and A. Cohen (to Hoffmann-La Roche, Inc.).
- (36) U.S. Pat. 2,443,473 (June 15, 1948), N. A. Milas (to Research Corp.).
- (37) U.S. Pat. 2,447,325 (Aug. 17, 1948), T. Y. Gallagher (to Research Corp.).
- (38) U.S. Pat. 2,576,486 (Nov. 27, 1951), J. L. Speier (to Dow Corning Corp.).
- (39) Brit. Pat. 541,138 (Nov. 13, 1948), F. Hoffmann-La Roche & Co. A.-G.
- (40) Brit. Pat. 588,833 (June 4, 1947), Resinous Products & Chemicals Co.
- (41) Can. Pat. 302,784 (Aug. 5, 1930), L. C. Swallen (to Commercial Solvents Corp.).
- (42) Jap. Pat. 153,150 (Nov. 21, 1942), Nippon Chemical Industries Co.

WM. HOWLETT GARDNER AND LAWRENCE H. FLETT

**SUCCINONITRILE**,  $\text{NCCH}_2\text{CH}_2\text{CN}$ . See *Nitriles and isocyanides*, Vol. 9, p. 369; *Succinic acid*.

**SUCCINYLCOLINE**,  $(\text{CH}_3)_3\text{N}^+\text{CH}_2\text{CH}_2\text{OOC}(\text{CH}_2)_2\text{COOCH}_2\text{CH}_2\text{N}^+(\text{CH}_3)_3$ . See *Stimulants and depressants of the nervous system*, p. 40.

**SUCCINYLSULFATHIAZOLE**,  $\text{C}_{13}\text{H}_{13}\text{N}_3\text{O}_5\text{S}_2 \cdot \text{H}_2\text{O}$ . See *Sulfa drugs*.

**SUCROSE**,  $\text{C}_{12}\text{H}_{22}\text{O}_{11}$ . See *Sugar manufacture; Sugars (commercial)*.

## SUGAR ANALYSIS

For analytical purposes, sugars are classified as reducing or nonreducing. All sugars are polyhydroxy compounds that either contain an aldose or a ketose residue, or are capable of forming such a group on hydrolysis. On this basis the former, that is, the aldoses and ketoses, are called reducing sugars, since they have reducing power, and the latter are nonreducing sugars. Solutions of a reducing sugar consist of mixtures of isomeric forms of the sugar, and the physical and chemical properties of the solutions depend upon establishment of an equilibrium. Nonreducing sugars exist only in one form, and, consequently, these solutions are stable. Glucose, fructose, lactose, and maltose are representative of reducing sugars, while sucrose is nonreducing. See also *Sugar manufacture*; *Sugars*.

## General Physical Methods

All sugars are white, crystalline, water-soluble substances. Optical rotation, density, refractive index, and viscosity measurements of their aqueous solutions are used for determining concentration of pure sugar solutions. In addition, optical rotation measurements of solutions of known concentration are a means of identifying the individual sugars.

**Optical Rotation.** (See *Polarimetry*.) The plane of polarized light is rotated to the left or to the right as it passes through a sugar solution. When measured under known conditions, the amount and direction of rotation is characteristic for each sugar and hence is a means of identification. Observed or direct rotations are converted to specific rotations by the formula:

$$[\alpha]_{\lambda}^t = \frac{\alpha}{l \times c}$$

where  $\alpha$  is the observed rotation (circular degrees),  $l$  is the length of tube containing the sugar solution (decimeters),  $c$  is the concentration (grams of sugar per 100 ml. solution),  $\lambda$  is the wave length (Ångström units), and  $t$  is the temperature (°C.).

Since aqueous solutions of the reducing sugars contain a mixture of their isomeric forms, optical rotation is constant only when equilibrium is established within the solution. The change in rotation that takes place while equilibrium is being established is called *mutarotation*. *Molecular rotation* is the specific rotation multiplied by the molecular weight. Specific rotations of many of the sugars are given under *Sugars*, p. 236.

The saccharimeter (see Vol. 10, p. 881) is a modification of the polarimeter specifically designed for the sugar industry. Direct readings on this instrument are used extensively throughout the beet and cane sugar industries for factory control and in trade transactions.

**Density (*q.v.*).** Density measurements are widely used in the sugar industry for the determination of sugar concentrations particularly in connection with transactions involving sirups and molasses. The term density represents mass per unit volume and is usually expressed in grams per milliliter. Closely related to density is specific gravity, which is a comparison between the masses of equal volumes of the substance in question and of water, the temperature of both being stated, as,  $d_{18}^{25}$ . Since at 4°C., the temperature of its maximum density, 1 ml. of water weighs 1 g., specific gravity  $d_4^t$  is numerically equal to density.



The following terms are used in the literature in connection with density measurements of sugars.

$$\text{True density} = \frac{\text{wt. of given vol. of soln. at temperature } t}{\text{wt. of same vol. of water at } 4^{\circ}\text{C. (weights in vacuum)}}$$

$$\text{Apparent density} = \frac{\text{wt. of given vol. of soln. at temperature } t}{\text{wt. of same vol. of water at } 4^{\circ}\text{C. (weights in air)}}$$

$$\text{True sp.gr.} = \frac{\text{wt. of given vol. of soln. at temperature } t}{\text{wt. of same vol. of water at temperature } t \text{ (weights in vacuum)}}$$

$$\text{Apparent sp.gr.} = \frac{\text{wt. of given vol. of soln. at temperature } t}{\text{wt. of same vol. of water at temperature } t \text{ (weights in air)}}$$

In order to facilitate the conversion of the density of a sugar solution to percentage sugar content, standard tables are available for use with the common sugar, sucrose, and with others such as glucose, maltose, and fructose. Because of its commercial importance, sucrose density tables have been prepared for use over wider ranges of temperatures and concentration than have those for the other sugars. In general, these tables apply to pure sugar solutions and the results obtained by their use are strictly correct only when they are thus employed. However, much of the material that naturally occurs along with a sugar is found to have a similar density. The tables are therefore useful for determining the concentration of various sirups and sugar mixtures such as molasses (*q.v.*). A comparison of the densities of 10% solutions of the following sugars when measured at 20°C. is indicative of the accuracy that can be expected when using the sucrose table for other sugars; arabinose 1.0379, glucose 1.0377, fructose 1.0385, galactose 1.0379, sorbose 1.0381, sucrose 1.0381, maltose 1.0386, lactose 1.0376, and raffinose 1.0375. Density measurements of sugar solutions are made by the methods generally applicable to the determination of densities of liquids. Hydrometers, graduated on the basis of percentage (by weight) of sucrose in a pure sucrose solution, are used by the sucrose industry. The graduations are referred to as *degrees Brix* and standardization is generally made at 20°C. A solution of 45° Brix therefore, has the same density as does a 45% sucrose solution. Hydrometers graduated in degrees Baumé are also used, particularly where molasses and sugar

TABLE I. Refractive Indexes of Sugar Solutions at 20°C.

g. sugar/ 100 g. soln.	Refractive Indexes					
	Sucrose	Glucose	Fructose	Invert sugar	Maltose.H <sub>2</sub> O	α-Lactose.H <sub>2</sub> O
0	1.33299	1.33299	1.33299	1.33299	1.33299	1.33299
10	1.34783	1.34775	1.34764	1.34764	1.34739	1.34758
20	1.36384	1.36356	1.36331	1.36341	1.36284	—
30	1.3811	1.38052	1.38029	1.38040	1.37947	—
40	1.3997	1.39872	1.39857	1.39866	1.39736	—
50	1.4200	1.41826	1.41817	1.41827	1.41659	—
60	1.4418	1.43918	1.43912	1.43928	1.43723	—
70	1.4651	1.46156	1.4615	1.46172	—	—
80	1.4901	1.48542	1.4851	1.48564	—	—
90	—	—	1.5100	—	—	—

TABLE II. Methods of Analysis for Reducing Sugars.

Method	Application	Reagent	Reaction conditions	Size of sample, ml.	Amt. of sugar in sample, mg.	Final determination
Munson and Walker	Glucose, fructose, invert sugar, lactose, and maltose	Soxhlet	Boil 2 min.	50	5-240	Gravimetric or volumetric determination of reduced copper
Quisumbing and Thomas	Glucose, fructose, invert sugar, lactose, and maltose	Copper-alkali-tartrate	30 min. at 80°C.	50	50-150	Gravimetric or volumetric determination of reduced copper
Lane and Eynon	Glucose, fructose, invert sugar, lactose, and maltose	Soxhlet	Boil 2 min.	0-50	100-800 mg./100 ml.	Direct titration of Soxhlet reagent with sugar soln.
Luff-Schoorl	Glucose, fructose, invert sugar, lactose, and maltose; invert sugar in presence of sucrose	Copper-carbonate	Boil 10 min.	50	2.4-62.2	Iodometric titration of reduced copper
Spengler, Todd, and Scheuer	Invert in beet sugars	Copper-tartrate-carbonate	10 min. in boiling water bath	100	0-20	Iodometric titration of reduced copper
Sichert and Bleyer	Glucose in presence of maltose	Copper-acetate	20 min. in boiling water bath	20	26.5-99	Dissolve reduced copper in ferric sulfate and titrate with permanganate
Ofner	Invert sugar in sucrose	Copper-tartrate-carbonate-phosphate	Boil 5 min.	5	1-20	Iodometric titration of reduced copper
Shaffer and Hartmann	Invert sugar in sucrose	Copper-citrate-carbonate	Boil 5 min.	50	15-150	Iodometric titration of reduced copper

Scales	Many sugars	Copper-citrate-carbonate	Boil 6 min.	10	10-20	Iodometric titration of reduced copper
Willstätter and Schudel	Aldoses	0.1 <i>N</i> iodine 0.1 <i>N</i> sodium hydroxide	Room temp.	Optional	1-100	Titration of excess iodine
Nyrs	Fructose	Copper-carbonate-bicarbonate	55°C.	20	0-92	Copper analysis
Somogyi	Glucose in blood	Copper-carbonate	15 min. in boiling water bath	5	0-2	Iodometric titration of reduced copper
Somogyi	Glucose; used for analysis	Copper-phosphate	10 min. in boiling water bath	5	0-3	Iodometric titration of reduced copper
Hagedorn and Jensen	Glucose in blood	Alkaline ferricyanide	15 min. in boiling water bath	12	less than 0.38	Iodometric titration of reduced copper
Folin and Malmros	Glucose in blood	Ferricyanide-carbonate	8 min. in boiling water bath	4	0-0.2	Read % transmission on a photoelectric colorimeter
Folin and Wu	Glucose in blood	Copper-carbonate-phosphomolybdic acid	8 min. in boiling water bath	2	0.8	Read % transmission on a photoelectric colorimeter
de Whalley	Invert sugar in refined sucrose	Methylene blue-sodium hydroxide	2 min. in boiling water bath	7 g. sucrose	0.001-0.15% invert sugar	Visually compare colors with standard color tubes
Anthrone	Glucose; can be adapted for other sugars	Anthrone-95% sulfuric acid	10 min. in boiling water bath	2.5	0-80 $\gamma$	Read % transmission on a photoelectric colorimeter

sirups of both sucrose and dextrose are concerned. This is an arbitrary scale which is related to specific gravity by the following equation:

$$\text{degrees Baumé} = 145 - (145/d_{20}^{20})$$

**Refractive Index.** (See *Refractometry*.) The index of refraction is another physical measurement that can be related to the sugar concentration of a solution, but since this relationship varies somewhat for different sugars, tables such as Table I have been constructed for a number of sugars of commerce. The most widely used of these is the "International Scale (1936) of Refractive Indices of Sucrose Solutions at 20°C", adopted by the International Commission for Uniform Methods of Sugar Analysis. For accurate work, such a table is strictly applicable only for solutions of the pure sugar upon which it is based. In less precise work, including commercial uses, the sucrose table may be employed with impure solutions and sugar mixtures for approximate values. Corrections have been devised to compensate for the effect of impurities, thus increasing the accuracy in such cases.

**Viscosity.** (See *Viscometry*.) The viscosities of sugar solutions are of concern to the sugar industry because of their effect on the rate of crystallization and on the washing of crystals. This property is also considered when designing pumps, pipe systems, and other equipment used for the handling of sugar solutions. Viscosities are measured by determining the rate of flow of a solution under specified and carefully controlled conditions, the rate of travel of a ball through a known distance in a medium whose viscosity is under investigation and by the so-called torsion viscometers. Sucrose solutions have been used as standards for calibrating viscometers. The unit of viscosity is the poise. At 20°C., the viscosity of water is 1 centipoise or 0.01 poise, while that of a 60% sucrose solution at 10°C. is approximately 1 poise. Viscosity tables for sucrose and for the dextrose industry are available.

### Chemical Methods for Reducing Sugars

The reducing action of the aldose and ketose sugars is the basis for a large number of methods that have been devised for their quantitative and qualitative determination. In general the reagents may be classified as alkaline copper solutions stabilized by tartrate, citrate, or carbonate ions; copper acetate; potassium ferrocyanide; tungstates; and phenolic reagents in strong acid solution. See Table II.

**Macro Methods.** The alkaline copper tartrate reagent devised by Fehling and modified by Soxhlet is used in a number of macro methods. The soluble copper-tartrate complex ion present in this reagent is deep blue in color. Cuprous ions resulting from reduction of the copper do not form a complex with the tartrate but are precipitated from the alkaline solution as cuprous oxide. Many methods using this reagent have been devised. They differ in time and temperature of heating, amount of reagent used, and method for the determination of the reduced copper. The method of Lane and Eynon is unique in that a measured quantity of sugar solution is added to the hot reagent until the copper is completely reduced. In the other procedures an excess of reagent is used, and the cuprous oxide is separated by filtration and subsequently determined gravimetrically or volumetrically. Details of these procedures and their applicability are to be found in the general texts on sugar analysis. The method of Lane and Eynon follows in detail. Although more rapid, this method

gives results whose accuracy compares favorably with other procedures using copper alkali reagent and consequently it has been generally adopted by industry.

**Lane and Eynon Method.** *Reagents:* Soxhlet's modification of Fehling's solution: (a) copper sulfate solution: dissolve 34.639 g. of pure  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  in water and dilute to 500 ml.; (b) alkaline tartrate solution: dissolve 173 g. of Rochelle salt and 50 g. of NaOH in water and dilute to 500 ml. (carbonate-free NaOH); (c) methylene blue solution: 1% aqueous solution.

*Standard method of titration:* 10 or 25 ml. of mixed Soxhlet's reagent is placed in a 300–400-ml. flask. The sugar solution is placed in a 50-ml. buret. The outlet of the buret must be so designed that neither the stopcock nor the sugar solution is heated by the steam evolved during the reaction. Almost the whole of the sugar solution that will be required to completely reduce the copper is added to the cold reagent. The additional sugar solution required should be 0.5–1 ml. The flask containing the reaction mixture is heated over an asbestos gauze plate. After the liquid has begun to boil, it is kept in moderate ebullition for 2 minutes, and then without removing from the flame, 3–5 drops of methylene blue solution are added, and the titration is completed in one additional minute, so that the reaction mixture boils for approximately 3 minutes without interruption. The intense blue color of the methylene blue indicator, in the absence of air, almost instantly disappears when excess reducing sugar has been added. Duplicate determinations should agree within 0.1 ml. in the volume of sugar solution required.

Usually the sugar concentration is not known with sufficient certainty to add the proper amount to the cold copper reagent. Consequently, Lane and Eynon advise performing a preliminary titration in order to determine the approximate volume of sugar solution required. This is most conveniently accomplished by adding an initial volume of 15 ml. of the sugar solution to the measured volume of the copper reagent, boiling for 15–20 seconds, and then adding further increments of sugar until the blue color of the copper solution has nearly disappeared. This point can be judged within 1 or 2 ml. of sugar solution. Methylene blue is then added and the titration completed dropwise, the period of operation occupying as close to 3 minutes as possible. In the analysis of solutions of hexoses, this incremental method is nearly as reliable as the standard method, but with solutions of the disaccharides it is desirable to repeat the titration by the standard method.

*Calculation:* Lane and Eynon determined the weight of each sugar required to reduce the copper completely. These weights, which vary with the nature of the sugar and with its concentration, constitute a table of factors (see Table III) from which the proper one may be selected when the titer is known. The concentration of sugar is then:  $(\text{factor} \times 100)/\text{titer} = \text{mg. of sugar in 100 ml.}$  It is desirable for the analyst to determine the factor for a known sugar solution similar to the solutions to be analyzed. In this way he may apply any slight correction that should be made to the tabulated factors. By properly diluting the solution under investigation so that the total volume at the end of analysis is the same as that when a standard solution is used (within 1 ml.), the titration may be converted directly to milligrams of sugar. This is the basis of the so-called constant volume modification. When sucrose is present, allowance is made for reduction due to its hydrolysis by including it in the standard. Tables for invert sugar in the presence of sucrose are also available.

TABLE III. Factors for Use with the Lane and Eynon Method.  
(25 ml. of reagent)

Titer, ml.	Sugar				
	Invert	Glucose	Fructose	Maltose	Lactose. $\text{H}_2\text{O}$
25	124.0	120.5	127.9	194.5	169.9
30	124.3	120.8	128.1	192.8	168.8

(For complete tables see standard reference books.)

Chemical methods have been developed specifically for determining small amounts of invert sugar in the presence of sucrose. The reducing power of sucrose in the presence of the hot alkaline Fehling's solution is greatly reduced when less alkaline copper solutions such as one of the copper carbonate reagents are employed. Methods of this type are Luff-Schoorl, Ofner, and the Berlin Institute. In all of the reducing

sugar methods the amount of copper reduced is empirical and depends upon detail of procedure.

A method based upon the reduction of methylene blue has been devised by de Whalley for determining invert sugar in refined sugars. This reagent, which is used as an indicator in Lane and Eynon's method, changes from a blue to a colorless compound in the presence of reducing sugars.

The copper-carbonate reagent devised by Benedict is generally used for the detection of glucose in urine and a procedure has been standardized for use of diabetic patients. (Benedict's solution: 17.3 g. of  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ , 173 g. of sodium or potassium citrate, and 100 g. of anhydrous sodium carbonate are dissolved in water and diluted to a final volume of 1 liter.)

Nyn's selective method for the determination of fructose is based upon the fact that, at  $55^\circ\text{C}$ ., fructose has thirteen times the reducing power of glucose when reacted with a copper-carbonate-bicarbonate reagent.

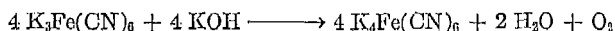
Aldoses react with iodine in dilute alkaline solution to form the corresponding monobasic acids while ketoses and nonreducing sugars are only slightly affected by this reagent. Advantage is taken of this fact in devising selective methods for glucose.

General information on reducing sugar methods is given in Table II. Detailed procedures are available in standard texts on sugar analysis.

**Micro Methods.** Micro methods of sugar analysis find their widest application in medical and biochemical laboratories; hence most of them have been standardized for glucose alone. They also are applicable to the analysis of macro samples containing micro amounts of the sugar in question. The determination of invert sugar in high-grade sucrose and the glucose end group in dextran represent the latter use.

Micro methods for the determination of reducing sugars fall into three major categories depending upon the type of reagent used: (1) the reduction of ferricyanide to ferrocyanide, (2) the reduction of cupric sulfate to cuprous oxide, and (3) the development of color when the sugar reacts with phenols in concentrated acid solution. As a rule the copper reagents are more selective in their oxidizing action on the sugars than are the ferricyanide reagents. The latter have the advantage of not being easily reoxidized by air.

Alkaline ferricyanide is reduced to ferrocyanide according to the following equation:



the reducing sugar reacting with the oxygen. The reaction is sensitive to changes in concentration, salts present, and pH; therefore, detailed procedures must be followed. The Folin-Malmros method based on that of Hagedorn and Jensen is extensively used. The latter authors treated the ferrocyanide formed by the reducing sugar with hydrogen iodide and titrated the iodine liberated with standard thiosulfate, while Folin and Malmros determine the reduction by use of a colorimeter.

Micro copper methods employ weakly alkaline copper reagents and in general are based on the same reactions as are the macro copper reduction methods. The reduced copper is determined colorimetrically or by iodometric titration.

In concentrated acid solution hexoses are converted to furfural derivatives which in turn react with phenolic reagents to form colored solutions. Anthrone belongs to

this class of reagents. The amount of sugar in a sample is correlated with the depth of color produced when the reagent is used according to specification.

Glucose dehydrogenase in the presence of oxygen converts D-glucose to D-glucono- $\delta$ -lactone. Because this enzyme is specific in its action it has been used for determining D-glucose in the presence of other sugars.

There are additional micro methods depending on other reagents, such as those of Summer using dinitrosalicylic acid, Lewis and Benedict using picric acid, and Benham and Despaul using molybdate, but these methods are not widely used. Details of procedure are to be found in the original literature as well as in the standard references on sugar analysis.

### Chromatographic Methods

Chromatographic techniques (see *Chromatography*) are utilized for the separation of sugar mixtures for both quantitative and qualitative analysis. Monosaccharides are eluted from columns made of Darco 60 and Celite (1:1) by water, disaccharides by 5% ethyl alcohol, while the higher sugars are removed by increasing ethyl alcohol concentrations. Mixtures such as corn sirups, honeys, and partially hydrolyzed polysaccharides have been separated into fractions by this procedure. Sugar cane juices have been studied by adsorption on fuller's earth-type clay and subsequent development with 95% ethyl alcohol. Zones of glucose and fructose are formed and from these the respective sugars are reclaimed by water elution. Sugar mixtures are separated on columns of powdered cellulose by the developers used in paper chromatography. Macro samples of carbohydrate mixtures can be separated into their constituents on such columns. Qualitative micro analyses of sugar mixtures are easily accomplished by paper chromatography. A large volume of literature has been published on the application of this technique to sugars and sugar derivatives. Developing solutions and colored indicators for location of the separated sugars vary with the requirements of the immediate investigation.

Paper chromatography is also used to separate small quantities of non-sugars. In this capacity it is used as an indication of purity. Raffinose, which is found in quantities of less than 1% in raw beet sugar, and which has considerable importance where the Steffen process is used (see *Sugar manufacture*) has been determined industrially by a paper chromatographic technique. Development of the chromatograph is accomplished by use of a 1-butanol, pyridine, water, benzene (5:3:3:1) mixture or by a 1-propanol, ethyl acetate, water (7:1:2) mixture. The sugar spots are located by spraying with an alcoholic solution of 1-naphthol to which phosphoric acid has been added.

### Analysis of Sucrose and Sucrose Products

**Sucrose**, a nonreducing disaccharide, hydrolyzes in acid solution or in the presence of enzymes to form equimolecular amounts of D-glucose (dextrose) and D-fructose (levulose). The optical rotation of a sucrose solution changes from a positive to a negative value during hydrolysis and hence the term inversion is applied to the process and the resulting D-glucose-D-fructose mixture is called invert sugar (see p. 251).

The Clerget method is generally used for determining sucrose. It is a polarimetric method in which the difference in optical rotation of the sample before and after

hydrolysis is translated into weight of sucrose. In its simplest form the Clerget formula is:

$$\% \text{ sucrose} = \frac{(P - P')100}{C + ac - b(t - 20)}$$

$P$  and  $P'$  are the direct and invert polarization readings in °S. (international sugar scale, see Vol. 10, p. 884) of a solution containing 26 g. of the material in question in 100 ml. solution;  $C$  is a constant known as the basic value of the Clerget divisor at 20°C.;  $a$  and  $b$ , respectively, are the change in value of the Clerget divisor with concentration and temperature; and  $c$  is the concentration in g./100 ml. of the solution whose optical rotation is being determined. When this is different from 26 g./100 ml., the values of  $P$  and  $P'$  are calculated by direct proportion. Approximate results are obtained by using the formula:

$$\% S = \frac{(P - P')100}{133 - 0.5(t - 20)}$$

The optical rotation is dependent to some degree on the salts present, the temperature at which hydrolysis takes place, and whether acid or invertase is used to bring about the inversion. The Clerget method has been the subject of a large number of investigations, with the result that numerous modifications have been devised. Specific details regarding these may be found in standard reference books on sugar analysis.

Sucrose is also determined chemically. On hydrolysis, nonreducing sucrose is converted into equal amounts of the reducing D-glucose and D-fructose or invert sugar. Impure sugar products, such as molasses, contain invert sugar along with sucrose. The difference in reducing sugar before and after hydrolysis results from hydrolysis of sucrose, and the latter may thus be determined. The strongly alkaline reagents attack the sucrose molecule to a degree depending upon the pH of the reagent and the time and temperature of the reaction. In making the final calculations this must be considered. Appropriate tables are available for use with the individual sugar methods when determining sucrose (see "Chemical Methods for Reducing Sugars").

**Invert Sugar.** Cane juice contains up to 1.35% of reducing sugars, D-glucose and D-fructose. Concentration of the juice and any subsequent hydrolysis of sucrose results in an appreciable amount of invert sugar in the final sirup. During crystallization the invert sugar concentrates in the molasses. The determination of invert sugar is discussed under "Chemical Methods for Reducing Sugars."

**Moisture.** The moisture content of solid sugar products may be expressed as such, but with semisolid and liquid products it is more frequently referred to indirectly and dry substance is reported. The following procedures are listed by the International Commission for Uniform Methods of Sugar Analysis as recommended procedures for the determination of dry substance in sugars and sugar products.

- (1) Density, using (a) pycnometer or density bottle or (b) hydrometer.
- (2) Refractive index.
- (3) Distillation with immiscible solvent.
- (4) Drying method at atmospheric pressure.
  - (a) Steam or boiling water ovens.
  - (b) Electrically heated ovens with or without fans.
  - (c) Passing heated air through a layer of sample.
  - (d) Silver-plate method of Rice and Baleracki.



- (5) Vacuum oven drying at low temperatures:  
 (a) Lobry de Bruyn method at 38°C. for 800–990 hr.  
 (b) I.C.U.M.S.A. standard method at 60°C.  
 (c) A.O.A.C. official method at 70°C.  
 (d) Corn Industries Research Foundation Method at 80°C.  
 (6) Karl Fischer titration.

A great deal of work has been done in devising techniques that will give accurate results, particularly when sugar sirups are concerned. In drying methods employing heat, the point at which loss of weight due to moisture stops and decomposition begins is difficult to determine. A curve based on loss of weight with time is useful in determining this point. After the moisture has been removed, decomposition appears as a gradual loss in weight and the slope of the decomposition curve increases with temperature. Conditions of heating for a specific length of time at a given temperature must be worked out for each product; hence the general procedure is to heat until constant weight is obtained. The details of procedure are available in the general handbooks on sugar analysis.

Refractive index and density measurements may be converted directly into per cent sugar, which is dry substance in the case of pure sugar solutions. If there are impurities present with refractive indexes or densities of approximately the same value as those of sugar solutions of similar concentrations, the physical measurements are converted to per cent dry substance and not to per cent sugar. These methods are frequently used in the case of liquid sugars (pure sugar solutions) and molasses.

The dextrose industry has used the distillation method for the determination of moisture in sirups. In this procedure the sample to be analyzed is introduced into a flask containing a weighed sample of dry Filter-Cel. Benzene is added and the contents of the flask are mixed thoroughly. The flask is joined to a condenser by means of a curved tube containing a trap into which the condensate falls. The flask is heated and the moisture from the sample is thus transported to the trap. Being immiscible with the benzene, it separates into a layer and is measured volumetrically by means of graduations on the trap.

The Karl Fischer titration method is based on the reaction of water with iodine and sulfur dioxide in solution in anhydrous pyridine and methanol (8). The amount of iodine consumed according to the equation:



is a measure of the water present. With proper precautions to eliminate all moisture except that in the sample accurate results are obtained.

**Ash.** The determination of ash in sugars and sugar products is subject to considerable uncertainty, yet it is widely used as an indication of the mineral products present. It may be determined gravimetrically by direct incineration, but in commercial practice the so called "sulfated ash" method is generally employed. In this, the sample is carbonized in the presence of sulfuric acid and heated in a muffle furnace at 550°C. After cooling, sulfuric acid is again added and the 550°C. heating is repeated. The weight of "sulfate ash" thus obtained is expressed as per cent. An arbitrary 10% deduction is sometimes applied to sulfate ash to correct to the approximate direct ash value. Since the magnitude of this correction varies greatly with different sugar products, the application of this correction is preferably avoided. When reporting ash it should be made clear as to whether double or single sulfuric acid addition was used and whether a 10% deduction was made.

Conductivity methods for determining mineral content and therefore ash are used extensively. The relation between ash as determined gravimetrically by the double-sulfate method and conductivity is constant for sugars of like origin and treatment. This is known as the C-ratio:

$$\text{Ash} = \text{C-ratio} \times \text{specific conductance}$$

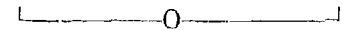
Size of sample, temperature, water correction, and type of product all must be considered when choosing the proper C-ratio. Details are to be found in standard sugar handbooks.

**Color.** (See *Colorimetry*.) Practically all of the color measurements in the sugar industry are made on solutions. The exception is the comparisons of colors of raw sugars in solid form. Light is transmitted through a sugar solution according to the Lambert-Beer law. It has been found that the ordinary coloring matter of sugar is such that sugar solutions appear brightest to the eye at a wave length of 560  $m\mu$ . For this reason, the International Commission for Uniform Methods of Sugar Analysis recommended in 1936 that the transmittancy be determined at 560  $m\mu$  (see Vol. 4, p. 268; *Turbidimetry and nephelometry*). The colors of sugar solutions are closely related to their turbidity, both being a matter of visual preception. Turbidity depends upon suspended matter while color is due to a colorant. Both properties are affected by their environment. Measurements of light transmission at two wave lengths, with proper interpretation, has been suggested as a means of compensating for turbidity in color measurements; and more recently an instrument has been used in which monochromatic light of three wave lengths is transmitted through the solution and the visual color computed from the readings. Details of procedure are to be found in the standard sources of information on sugar analysis.

Visual comparisons of the color of sirups are also used by industry, and standards are available for this purpose. These include colored glass plates as used by the maple sugar industry, caramel solutions of varying concentrations, mineral salt solutions, and oils. Freshly prepared solutions whose colors have been measured on a spectrophotometer may also be used for visual comparison. Because of the simplicity of their application, these visual measurements have not been entirely superseded by more accurate spectrophotometric methods.

### Special Methods

Sugar oxidation by means of periodic acid and of lead tetraacetate is used for analytical and for structural studies. Oxidation takes place where adjacent hydroxyls are found. With both reagents *cis*-glycols are more rapidly oxidized than are *trans*-glycols. Glucose, for example, consumes five atoms of oxygen and produces one mole of formaldehyde and five moles of formic acid. The reaction stops when a carbon atom is reached that does not carry an unsubstituted hydroxyl, an amino, or a carbonyl group. Thus glycosides form dialdehydes of the following type:  $\text{CHOR}.\text{CHO} \dots \text{CHO}.\text{CH}.\text{CH}_2\text{OH}$ , where the dotted line represents the former



position of a carbon atom that has been oxidized completely.

The formation and identification of sugar derivatives are used in analytical procedures. In some cases, rates of formation under specified conditions as well as the determination of physical constants of the compounds formed are used. The forma-

tion of osazones and hydrazones (see *Carbohydrates*, Vol. 2, pp. 869, 873; *Hydrazine*), glycosides, acetates, and methyl derivatives are among those employed for the identification of sugars. Methylation followed by hydrolysis to form partially methylated monosaccharides has been used extensively for the determination of polysaccharide structures. Propyl derivatives have been thus employed by the starch industry. Both propyl and methyl derivatives are distillable and the latter have also been separated chromatographically.

### Bibliography

- (1) A.O.A.C., *Methods of Analysis*, 7th ed., Washington, D.C., 1950.
- (2) Bates, F. J., et al., "Polarimetry, Saccharimetry and the Sugars," *Natl. Bur. Standards (U.S.), Circ.*, C440 (1942).
- (3) Binkley, W. W., and Wolfrom, M. L., *Chromatography of Sugars and Related Substances* (Scientific Series No. 10), Sugar Research Foundation, N.Y., 1948.
- (4) Block, R. J., LeStrange, R., and Zweig, G., *Paper Chromatography: A Laboratory Manual*, Academic Press, N.Y., 1952.
- (5) Browne, C. A., and Zerban, F. W., *Sugar Analysis*, Wiley, N.Y., 1941.
- (6) Hawk, P. B., Oser, B. L., and Summerson, W. H., *Practical Physiological Chemistry*, Blakiston, Philadelphia, 1947.
- (7) International Commission for Uniform Methods of Sugar Analysis, "Report of Proceedings of the 10th Session (1949)," *Internatl. Sugar J.*, 52, 169, 235 (1950).
- (8) Mitchell, J., Jr., and Smith, D. M., *Aquametry: Application of the Karl Fischer Reagent to Quantitative Analysis Involving Water*, Interscience, N.Y., 1948.
- (9) Spencer, G. L., and Meade, G. P., *Cane Sugar Handbook*, 8th ed., Wiley, N.Y., 1945.

EMMA J. McDONALD

## SUGAR MANUFACTURE

Sugar is the common name of the disaccharide sucrose (see *Carbohydrates; Sugars*). For the purpose of establishing standards of identity for foods, the United States Food and Drug Administration has defined the term sugar as "refined sugar (sucrose)." Refined sugar is one of the purest of all substances produced in comparable volume, being about 99.9% sucrose. Its commercial sources are the sugar cane and the sugar beet. When properly refined, the products from these two sources are, for practical purposes, identical in purity and physical characteristics.

In the manufacture of cane sugar, a raw sugar containing about 97% sucrose is produced in semitropical regions where the cane is grown and then refined, usually in countries where large quantities of refined sugar are consumed. Refined beet sugar, however, can be made directly from the beet, without first producing a raw sugar and is invariably so made in the United States and Canada, although in Europe the old process of producing raw beet sugar and refining it still persists.

Other commercial forms of sucrose, differentiated by prefixes to denote their origin and characteristics, are maple sugar, sorghum sugar in sirup form, and brown or "soft" refined cane sugar. Certain other commercial sugars, which require a prefix to distinguish them from sucrose, are corn sugar (dextrose, *q.v.*), milk sugar (lactose, see *Dairy products (by-products)*), and malt sugar (maltose). See also *Sugars (commercial)*.

Sucrose, accompanied by lesser amounts of D-glucose and D-fructose, occurs in the juices of many plants in addition to those that have been mentioned as commercial sources.

For the chemical and physical properties and analysis of sugar see *Carbohydrates*; *Sugar analysis*; *Sugars*.

Sugar is used primarily as a food and is one of the lowest in cost per calorie of energy furnished. It has also limited industrial applications, notably in the tobacco industry and in the manufacture of derivatives (see *Sugars and sugar derivatives*). Much research work has been and is being conducted in this latter field in order to discover new outlets for sugar, the world productive capacity for which exceeds present demand. Although sucrose has several practical commercial uses additional suggestions have been made for its use in the plastics field, among which are as a component of urea-formaldehyde resins and as an accelerator in the copolymerization of butadiene and styrene. Sugar cane wax can be obtained as a by-product of raw sugar manufacture. (See *Waxes*.)

The origin of sugar cane is lost in the myths of antiquity. Deerr (3), however, is of the opinion that it originated in the South Pacific and reached India in very early times, being mentioned in Indian writings long before the Christian era. The sugar cane was brought to China, probably about 100 B.C., and eventually was carried to northern Africa by the Arabs, whence it spread to southern Europe. Columbus brought it to the West Indies and planted cuttings of the cane. In the course of time it reached South America and Mexico; Jesuit missionaries carried cane to Louisiana in 1751. The manufacture of raw sugar in the Americas had reached large proportions by the eighteenth century and the application of the centrifuge in the manufacture of raw sugar in the nineteenth century made possible the present easily refined centrifugal sugars. The first sugar refinery in the United States appears to have been that of Nicholas Bayard, established in 1730 to supply "double and single Refined Loaf Sugar, as also Powder and Shop-Sugars, and Sugar-Candy." About one hundred years later the new "steam refining," using boneblack and vacuum boiling, was introduced, and shortly after the Civil War centrifugal machines came into general use, supplanting the laborious and time-consuming processing into sugar loaves. With these improvements and the consolidation of refineries that followed in the eighties and nineties, the modern cane sugar refining industry emerged. Subsequent improvements have been far reaching, but mainly along the lines of materials handling. The basic improvements have been the substitution of pressure filters for the old bag filters and to some extent clarification by flotation.

The early refineries of the U.S. obtained their supplies of raw sugar from the West Indies. The first commercially successful production of raw sugar in the U.S. was achieved by Etienne de Bore in Louisiana in 1791.

The use of beet sugar is comparatively recent. Beets have been cultivated since before the Christian era, but it was not until 1747 that Andreas Marggraf of Germany demonstrated that sugar is contained in the juice of the beet. Forty years later a pupil of Marggraf, Karl Achard, succeeded in increasing the sugar content of beets by cultivation, and made beet sugar in something like a practical way. Friedrich Wilhelm III of Prussia provided Achard with the means for building a beet sugar factory in 1802. By 1811 it had become evident that beet sugar manufacture could be made a successful undertaking. In that year, Napoleon Bonaparte, finding France's sugar supply cut off by the British blockade and as a result of his own prohibition of imports from any part of the British Empire, issued an edict to establish a beet sugar industry in France. The industry grew steadily in Europe until, just before World War I, most of the continental countries were producing enough beet sugar for their domestic needs and some had a surplus for exportation. Recovery after World War I was fairly rapid until again interrupted by World War II, but meanwhile Great Britain and Eire had established their own beet sugar industries as a protection in some measure against possible future wars which might cut off their overseas supplies.

The first beet sugar enterprise to achieve success in the U.S. was started by E. H. Dyer at Alvarado, California, in 1879. Slowly at first and later rapidly, with the encouragement of bounties, tax exemptions, and protective tariff duties levied upon imported sugar, the U.S. beet sugar industry expanded through California, the Rocky Mountain states, and the Great Lakes area.

By 1897 the world's beet sugar production had grown to a proportion substantially equal to that of cane sugar, and this position was maintained until the beginning of World War I (see under "Legislative and Economic Aspects"). Two factors were mainly responsible: the gradual abolition

of slavery in the cane-growing countries and legislative encouragements for beet sugar through protective tariffs and bounties. World War I had a disastrous effect on beet sugar production. Conversely, the cane sugar countries (notably Cuba and Java) stepped up production rapidly to meet the deficit in beet sugar. World War II seriously affected both cane and beet sugar production. Japanese occupation of Java and the Philippines was the major factor affecting cane sugar. As for beet sugar, some of Europe's most productive lands once again became battlefields.

## Cane Sugar

### CULTIVATION

The sugar cane is a grass of the genus *Saccharum*. Until comparatively recent times all cultivated cane was of the species *S. officinarum*, which existed in numerous varieties throughout the semi-tropical regions of the earth. It was once believed that the flower of the cane was sterile, but it was later discovered that the plant could be propagated from its seed. In 1889 this discovery was practically applied and led to the production of many hybrids, most often by crossing *S. officinarum* with certain wild canes in efforts to obtain resistance to disease and insect pests, as well as a greater yield of cane per acre, higher sucrose content, and certain other characteristics (15). Much of the world's sugar cane today consists of such hybrid varieties.

Sugar cane is planted before the close of the dry season and grows luxuriantly during the ensuing wet season. The planting consists of dropping cuttings of the cane about a foot long into shallow holes or furrows some 3 or 4 ft. apart and lightly covering with earth. Buds on the nodes quickly sprout and a clump or stool of cane develops from each cutting. The canes may grow to a height of 15-18 ft. The plants mature as the dry season approaches; sucrose is formed by photosynthesis. Harvesting time varies greatly in different parts of the world, according to climatic and other conditions. In Cuba and Puerto Rico, for example, the growing time is about 10-12 months and harvesting commences in December or January, continuing until May or June. In Hawaii, the cane is allowed to grow for an average of 22 months and the harvesting period is January-November. In Louisiana, because of possible freezing, the cane cannot be planted until March and harvesting is started in October of the same year and must be completed in January at the latest. When ready for harvesting, the canes, which may be 1-2 in. thick (most present varieties have stalks 1-1½ in. thick) and are unbranched, although clothed in broad leaves 3 ft. or more in length, are generally cut by hand close to the ground with a knife. The tops, which contain but little sugar, are lopped off and the leaves are stripped from the stalk.

A fairly recent innovation, especially where field labor is costly, is the machine harvester. Several types have been developed and are in practical use, chiefly in Hawaii and Louisiana. Disadvantages of machine harvesters are that the leaves are not completely removed and that considerable earth and stones are picked up by the mechanism along with the cane.

Sometimes (in Hawaii and Australia it is general practice), cane fields are burned over before the cane is cut. This makes hand harvesting less laborious and results in cleaner cane if machine harvested. Burned cane must be ground promptly, however, in order to forestall the rapid deterioration to which it is subject.

The cane is transported from field to factory by various means in different localities: by ox- or mule-drawn carts directly or to railroad loading stations and thence to the mill, by tractors pulling carts or large trailers, by flumes, or by waterborne barges.

Diseases of the sugar cane, notably the mosaic disease, have made severe inroads at times in cane-growing countries. In the 20th century, the very existence of the sugar industries of the Argentine, Puerto Rico, and Louisiana has been threatened by the prevalence and severity of the mosaic disease, so-called because of the spotted appearance of affected leaves. A change to resistant varieties of cane was the effective remedy in each case. Similarly the ravages of insect pests have at times been serious. In Hawaii in about 1908 the adventitious importation of a cane pest (a beetle) threatened the local industry with extinction. Eventually a parasite was found which was brought to Hawaii and proved effective in controlling the beetle.

### MANUFACTURE (RAW SUGAR)

In the U.S., sugar cane is grown in the Gulf states and Georgia, and raw sugar is manufactured only in Louisiana and Florida. The manufacture of raw sugar as it is

conducted in Cuba is here described as being typical (5) (see Fig. 1). Cane, arriving by rail, is first weighed on track scales. The cars are then tilted so that the cane

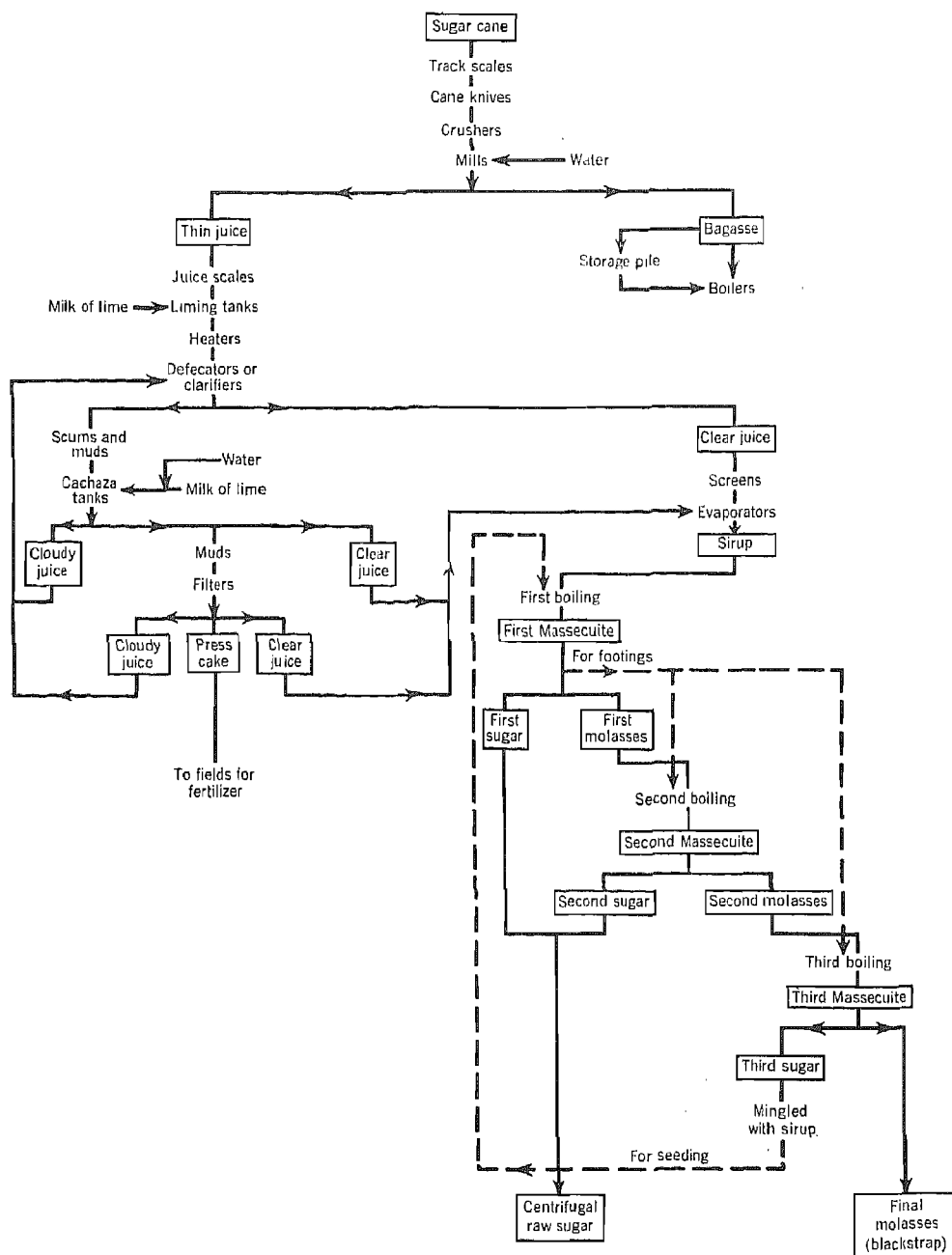


Fig. 1. Flow sheet of manufacture of raw cane sugar.

slides on a slatted conveyor that carries it to the cane knives. These cut the stalks into short pieces, after which they pass to the crushers. These consist of two cylinders

with interlocking ridges, which rupture cane by twisting as it passes through, thus preparing it for subsequent extraction by the mills.

**Extraction.** Each mill consists of three rollers, and a series of from four to seven mills is known as a tandem. Rollers are generally 84 in. long by 38 in. in diameter. Deep grooves every 4 or 5 in. permit the escape of juice, which is also aided by longitudinal intersecting grooves at a slight pitch. Pressures up to 550 tons are hydraulically applied to the top rollers.

As the cane passes through the mills, the plant cells are ruptured and the juice is expelled. As the blanket of cane leaves the second and third mills from the last, water (imbibition water) is sprayed on it, which, being absorbed by the expanding fiber, mixes with the remaining juice and facilitates its extraction by the last two mills. For the same purpose the juice from the last mills in the series is returned behind the forward mills, the juices from only the latter leaving the system. The pulp that is expelled from the last mill, known as *bagasse* (*q.v.*), is conveyed to the boilers, and, in well-designed factories, provides all the fuel that is required for operation. Modern factories even have an excess of bagasse, the disposal of which becomes a problem. In Louisiana bagasse is sold for the manufacture of an insulating fiber board which is used for interior walls of buildings and other purposes. In such cases the factory uses oil or natural gas for fuel. About 4% of the sugar present in the cane is lost in the bagasse.

**Clarification.** The cane juice as it flows from the mills is strained through screens to remove fine particles of bagasse. It is then subjected to the process of clarification (defecation), which generally consists of some combination of heating and treatment with lime. The sequence of operations, the number of separate additions of lime, and the form of the lime (slurry, dry, hydrated, or oxide) have been varied considerably. In many mills a preliminary addition of calcium hydroxide is made to partially neutralize the juice, which originally has a pH of between 5.0 and 5.5. The juice is then weighed, heated to near boiling, and perhaps then treated with additional lime. The hot juice, containing coagulated colloids and precipitated calcium salts, is passed into clarifiers (defecators), which are settling tanks with inclined or conical bottoms and outlet cocks at various elevations on the side. Here the juice is allowed to stand for about 45–90 minutes. Fine particles of fiber and other particles of low specific gravity, entangled with air, rise to the surface as a scum, while the heavier insolubles settle out as a mud at the bottom. The central portion, consisting of clear juice, in so far as possible is drawn off through the side outlets.

*Continuous clarification* in tray-type settlers, such as are used in mining operations and many chemical plants, is a development that has found wide acceptance. A system known as compound clarification, which employs these continuous clarifiers, permits separate treatment of the juices from different mills, which differ somewhat in purity. The juices from the crusher and first mills, after liming, are settled in a primary clarifier, the mud from which is mixed with the juice from the second mill, limed to a pH between 7 and 8, and settled in a secondary and smaller clarifier, while the clear primary juice goes to the evaporator. Juices from the remaining mills are used for imbibition. The secondary clear juice is returned to the primary clarifier and the secondary mud is filtered. The filtrate is mixed with secondary clear juice, while the cake is discarded. The principal advantage claimed for compound clarification is better elimination of colloidal nonsugars, with greater increase in juice purity, as compared with single clarification.

The scums and muds, collectively known as *cachaza*, are generally washed by some suitable process and the washings returned to the clarification stage. The mud or filter cake, is generally used as fertilizer on the cane fields.

**Crystallization and Recovery.** The clear juice is evaporated to sirup (*meladura*), generally in quadruple-effect evaporators. The sirup is maintained at such a density that only slight additional evaporation is necessary to bring about crystallization of the sugar it contains. This sirup passes next to single-effect vacuum pans, which may be of either the coil or calandria type. The calandria pan, however, is gradually replacing the older coil pans. The necessary heat is generally supplied by exhaust steam of, say, 8 p.s.i., but with the high vacuum that is maintained in the pans, ebullition is sufficiently rapid that there is active circulation of the contents. As water is boiled away, the sirup becomes supersaturated and the pan grains, that is, myriads of minute sugar crystals appear throughout the mass. It is a common practice to induce the formation of grain by shock seeding, which consists of drawing a small quantity of sugar dust into the pan when the sirup has reached the proper degree of supersaturation. The sugar boiler's art consists in allowing sufficient crystals to form so that when these have grown to the proper size by the continued evaporation of water and deposition of sugar on the original nuclei, more and more sirup being added as the water is boiled away, the pan will be full, and at the same time its contents of crystals and mother liquor will be as dense as practical. Uniformity of grain size and proper density of the crystal magma or *massecuite* (which, when boiling is stopped, should contain not more than about 10% of water), are of primary importance on account of their controlling influence on the yield of sugar crystals obtained. At the temperatures at which boiling and subsequent centrifuging operations are conducted, each additional pound of water in the magma will prevent about three pounds of sugar from crystallizing. When the boiling operation is completed, the vacuum is broken and the massecuite is allowed to drop through the foot valve of the pan into tanks with stirring arms, called mixers. From these it is fed by gravity into centrifugal machines. The *centrifuges* (centrifugals) are cylindrical baskets, commonly 40 in. in diameter and 24–30 in. deep, with perforated side walls, which are caused to revolve at a speed of 1000 to 1200 r.p.m. by means of direct-connected motors or belt drives. See Vol. 3, pp. 510–12.

The proper quantity of massecuite is run into the basket of the machine, usually while the latter is revolving slowly, and the machine is then speeded up to about 1100 r.p.m. When all removable molasses is out, a brake is applied and when a low speed has been reached, the bottom plate or valve is lifted and the sugar, called *first sugar*, is removed with an unloader that has a plowing action. The molasses drains away into an inclined gutter and thence to a tank. It is called *first molasses*.

A modern development is the self-discharging centrifugal machine, and a still later development is the high-speed centrifuge which is not self-discharging. This type in many instances is replacing both old-type and self-discharging machines. The baskets are designed for an operating speed of 1600–1800 r.p.m. and even higher. High-speed centrifuges are especially valuable for low-purity massecuite, since the time required for spinning is cut to a fraction.

The first molasses still contains considerable crystallizable sugar. It is returned to the pan for further evaporation of water in a second boiling operation and so again reduced to a massecuite, from which a crop of *second sugar* and *second molasses* are recovered by centrifuging. The second molasses still contains some crystallizable sugar and accordingly is returned to the pans for a third boiling. The nonsugar con-



centration of these final strikes, however, is so great that the growing of crystals proceeds at a very much slower rate than during the first and second boiling, and the material dropped from the pan is decidedly supersaturated. Accordingly, in order to make the recovery of sugar as complete as possible the third or final massecuite is dropped into crystallizers. These are usually cylindrical tanks containing 1000–1200 cu.ft., set horizontally, and are often equipped with water jackets or coils for cooling, and always with stirrers. Here the massecuite is gradually cooled with slow agitation. As a result, additional sugar which had been held in solution is deposited on the crystals already formed in the pan. Upon centrifuging the third massecuite, a *third sugar*, and *third or final molasses* are obtained. The latter, which is known as *blackstrap molasses*, is held in storage tanks and eventually sold, largely as an ingredient in cattle foods as well as for alcohol manufacture (see *Molasses*).

The third sugar is mingled with sirup from the evaporator and the resulting magma is either returned to the vacuum pans as a nucleus on which grain is built up in the first and second strikes, or it may be respun in centrifuges. In the latter case the resulting double-purged sugar is mixed with the first and second sugars. The first and second sugars are invariably mixed together and, whether or not any doubled-purged sugar is admixed, the final mixture is run into storage bins and eventually bagged out, or in some cases shipped in bulk form. This product is known in the trade as *centrifugal raw sugar* or simply "*centrifugals*."

The bags used for packing centrifugals are of jute and vary in size from a content of 330 lb. as in Cuba to as low as 100 or 105 lb. in Hawaii. Bulk shipment of sugar is increasing, particularly where factory and refinery are under one ownership or control, as in the case of raw sugar factories in Hawaii and a large refinery in California. Similar relations exist between certain Cuban and Puerto Rico factories and refineries in continental U.S. In such instances the factory may be provided with trucks or railroad cars for transportation to the shipping port where the sugar is loaded into vessels in bulk, as in the shipment of grain and some other commodities.

Centrifugal sugars have an average polarization close to 97° and contain about 1% of reducing sugars, less than 1% of moisture, a small amount of insolubles, and about 0.5% of ash. The undetermined difference from 100% is referred to as organic nonsugars. The final molasses contains about 35% of sucrose which is held in solution by the accompanying nonsucrose solids.

Methods have been suggested from time to time for the further extraction of sugar from blackstrap, but none has achieved sustained commercial use. The large content of reducing sugars precludes the application of the Steffen process, as practiced in the beet sugar industry. The methods which have been developed for recovery of sugar from cane molasses depend upon the destruction of the reducing sugars in order to make possible the precipitation of the sucrose as calcium saccharate in sufficiently pure form, as in the Steffen process, see p. 221, or as a saccharate of barium or strontium.

*Turbinados* is the name applied to a direct-consumption sugar made by washing centrifugal raw sugar with a water spray while spinning in the machine, then drying it with a jet of steam. The resulting product is decidedly off-white and contains necessarily most of whatever insoluble matter was present in the raw sugar, although its polarization generally exceeds 99°.

#### REFINING

The U.S. refineries, in addition to the moderate mainland crop of Louisiana and Florida, receive their raw sugar principally from Cuba, Puerto Rico, Hawaii, and the



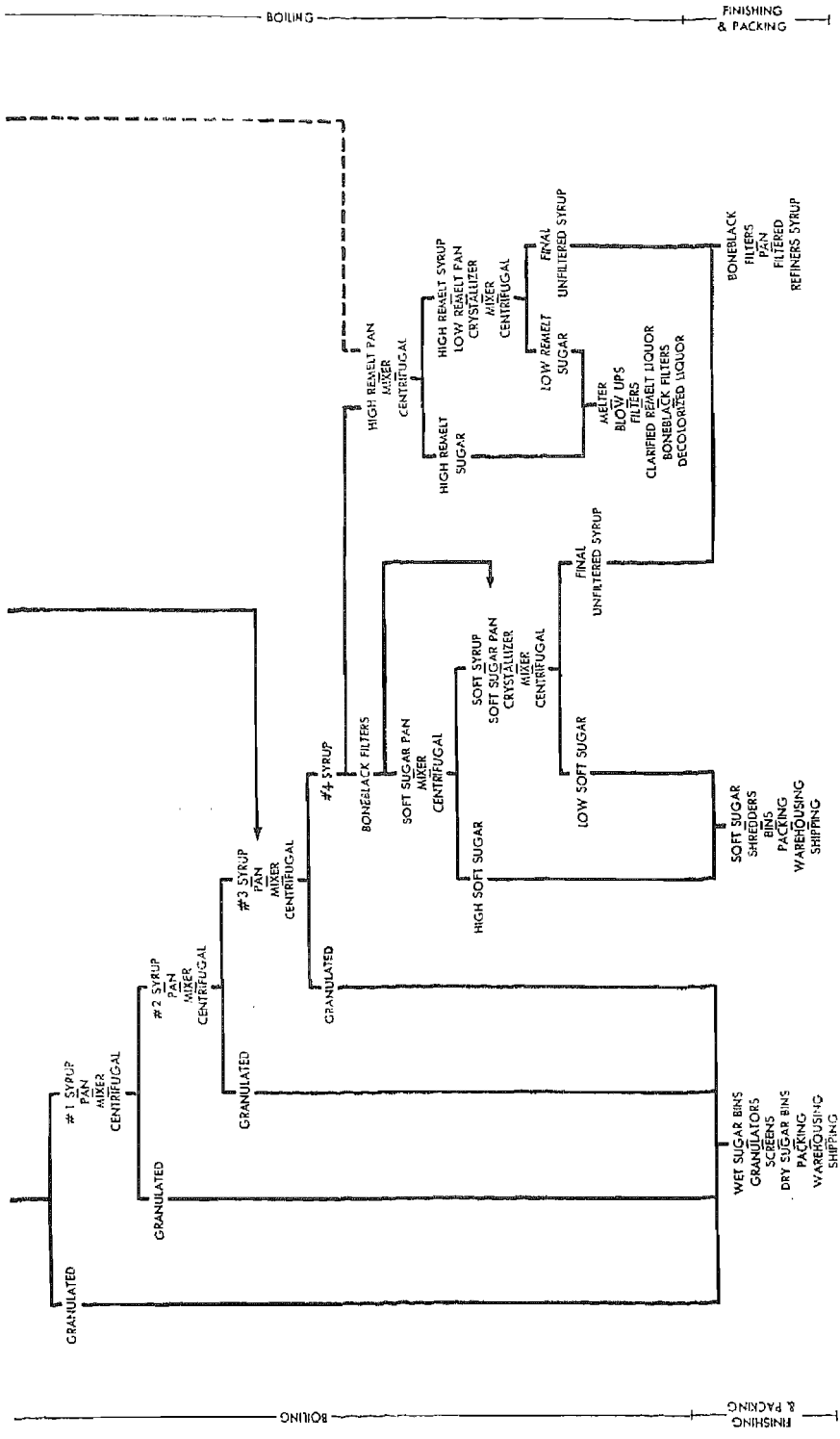


Fig. 2. Flow sheet of cane sugar refining.

Philippines, with minor amounts from the Dominican Republic and other countries. The centrifugal raw sugar, on arrival at the refinery (which is usually located on the waterfront of a good harbor) is weighted, sampled, and tested by the polariscope (saccharimeter) to determine its selling price, which varies from a base according to its polarization or "test." The duty rate of dutiable sugar is similarly determined.

**Washing.** The first step in the refining process, called *affination* or washing, separates the coating of molasses or mother liquor that surrounds the crystals of raw sugar. The sugar is first mingled in a long scroll conveyor with washings from previously affined sugar. The resulting pasty mass, called "magma" or "fillmass," is whirled in a centrifuge, the contents of the basket being sprayed with pure water. The liquid portion is thrown off and collected, while the sugar crystals remain against the perforated lining of the basket. At this point the sugar has a purity of 99°. The washed sugar, after it is dropped from the centrifugal basket, is "melted" (dissolved) in hot "sweetwater," a dilute sugar solution that results from some washing or sugar-dust collecting process in the refinery. The density of the solution is adjusted to 60–65% solids.

**Defecation.** The melted washed sugar (liquor) is pumped to tanks called "blow-ups" in which defecation is conducted. The pH of the liquor, which is slightly acid, is adjusted to the neutral point by the addition of milk of lime. Diatomite is then added as a filter aid, and after further agitation the liquor is run through leaf pressure filters. The effluent, while brilliantly clear, still has a strong yellow color, since little other than the insolubles has been removed at this point. The cake deposited on the filter leaves is "sluiced" off with hot water, the sluicings being filtered on a rotary suction filter or plate-and-frame filter presses. The sweetwater so obtained is used for melting purposes, and the final press cake is either regenerated by calcining for re-use or, in some refineries, discarded. The regenerated earth is less efficient as a filter aid than new earth and therefore must be applied in larger quantity, but regeneration is nevertheless economical when used on a large scale.

A part of the washings (*affination sirup*) from the raw sugar is returned for mingling with more raw sugar. The excess is either sent to the remelt department, where it is boiled into sugar that resembles raw sugar, which is remelted and refined, or a part or all of the excess sirup (about 80° purity) may be refined separately from the washed sugar, as shown in Figure 2.

Another process for defecating the washed sugar liquor, in use in several refineries in the U.S. and Canada, is treatment of the heated liquor with phosphoric acid and lime in a long, shallow tank while the heated contents are being impregnated with fine bubbles of air, introduced at the bottom. The precipitate of calcium phosphate, together with occluded insolubles and nonsugars precipitated from the liquor, is carried to the top to form a scum, which is drawn off by mechanical means. The scums must be filtered to recover the sugar contained therein, but filtration of the liquor itself is eliminated. This process has not come into general use in the industry, apparently because, although it is superior as to removal of colored and other soluble impurities, there is some apprehension as to destruction of sugar by inversion during the process.

In Europe (especially the United Kingdom) still another process, that of *carbonation* (carbonatation) (see p. 219), as employed in beet sugar manufacture, is practised. This process supplants defecation and reduces the amount of subsequent boneblack filtration that is required, since carbonation removes a very considerable proportion of the color from the liquor (6).

**Char Filtration.** The major purification of the liquor is effected by percolation through granular animal charcoal (boneblack or bone char). Boneblack adsorbs impurities, including coloring matter and mineral salts, from the sugar liquors. This process of purification, generally called char filtration, is carried on in large cylindrical cisterns known as char filters, each of which is approximately 10 ft. in diameter and 20 ft. deep, and almost completely filled with boneblack. The liquor is run on at the top, passes through the entire column of char, and emerges nearly colorless. It continues to run practically colorless for some hours, passing to a straw shade and eventually to yellow as the adsorptive capacity of the char gradually nears exhaustion. When a filter is completely exhausted, the liquor is displaced by water from the top downward, the effluent of constantly decreasing density being subsequently evaporated in multiple-effect evaporators, until a point is reached where sugar recovery by evaporation is no longer profitable. The filter is then washed with water for several hours, whereby most of the adsorbed mineral salts are removed. The char is finally dried and heated to redness in closed retorts to destroy the remaining organic impurities and to restore its adsorptive quality. Boneblack can be re-used many times in this way, its total life being from three to five years.

The application of **activated vegetable carbons** in refining has developed since about 1910. Such carbons have been made from peat, waste liquor from paper manufacture, and other carbonaceous materials (see Vol. 2, p. 881), and used to replace or augment boneblack as a decolorizing agent (2,10). Their color-removing power is far greater, weight for weight, than that of boneblack, but carbons remove little of the mineral salts and therefore do not materially reduce *melassigenic* effect (tending to prevent sugar crystallization). First cost of the adsorbent is higher and regeneration losses are much higher than for boneblack. The cost of an installation to handle the large quantity of boneblack for a refinery of comparable size, however, far exceeds the cost of a carbon installation. Largely for that reason, carbons have been adopted in a number of small refining enterprises, especially where cane is grown and the refinery adjoins a raw sugar factory. Carbon is also used as an auxiliary in boneblack refineries, mainly in connection with the manufacture of liquid sugar.

The application of activated carbon consists usually of a two-stage, counter-current treatment of the defecated, press-filtered, washed sugar liquor with the carbon in tanks equipped with agitators. The liquor is first treated with once-used carbon and press-filtered, the press cake being either regenerated or discarded. The clear liquor from the first carbon treatment is treated again, this time with fresh carbon, followed by filtration, and the press cake is returned for first treatment of more liquor. Regeneration generally involves burning in a rotary kiln with admission of restricted and carefully controlled amounts of steam and air, followed by treatment with hydrochloric acid and neutralization with caustic soda. Wherever carbons are used, the steps of the refining process, other than adsorbent treatment, are the same as in the older, standard process of boneblack refining.

A still later substitute for boneblack refining is **decolorization with hypochlorites**. Such a process is used to a considerable extent in refining operations conducted at raw sugar factories. The washed raw sugar is melted at a much lower temperature than usual (about 110°F.) and a solution of calcium hypochlorite and sodium phosphate is added to the liquor, which is run through a clarifier of the continuous, aerated type. Filtration of the clarified liquor through cloth, using a small amount of filter aid, is

generally necessary to achieve brilliance. Treatment of the filtered liquor with sodium hydrosulfite to remove any residual chlorine is recommended.

Purification of sugar juices and liquors by **ion exchange** (*q.v.*) has received attention in both the cane and beet sugar industries. The earlier ion-exchange agents, such as natural or artificial zeolites, which are useful for softening water, were found to be of little value in sugar refining since the result is merely the substitution of one metallic cation for another in the solution treated as, for example, sodium for calcium. Thus, there is substantially no removal of mineral substance from an impure sugar solution and, consequently, substantially no reduction in melassigenic effect. It was not until after the development of synthetic cation and anion resins about 1935 (1) that extensive studies were made of the possibilities of sugar purification by ion exchange. It has been found that certain synthetic cation resins of the phenolic type, as well as some sulfonated polystyrenes, are capable of removing practically all of the mineral matter from both cane and beet juices. The hydrogen ions substituted for the metallic cations render the solution strongly acid, so that the treatment must take place at a comparatively low temperature in order to prevent excessive inversion of sugar, if a crystallized product is sought. The treatment with an anion resin, usually an amine derivative, which follows, causes the free mineral and organic acids left in solution by the cation resin to be either adsorbed or combined by a true exchange reaction with the anion resin. The net result of the entire process is the removal from solution of mineral and organic acid salts, together with other substances, including coloring matter. The removal of organic nonsugars is not nearly so complete as in the case of the ash or mineral matter, but is nevertheless considerable. Regeneration of the resins, the cation exchanger with sulfuric acid and the anion resin with caustic soda or ammonia, is simple, although expensive compared with the regeneration of boneblack.

Ion exchange has been applied on a factory scale in all three branches of the sugar industry: raw cane sugar manufacture, cane sugar refining, and beet sugar manufacture. The problems have been many and in some instances grave, not the least of them being the difficulty of keeping the inversion of sugar to a practical minimum in the strongly acid cation exchanger effluent. Cane juice has been treated on an experimental factory scale with the production, without further refining, of granulated sugar. In beet sugar manufacture (8), purification by ion exchange has been practiced in several factories and many data have been accumulated and published (11). The refining of raw cane sugar into a crystalline product, employing ion exchange, has not yet been accomplished on a commercial scale. Its possibility appears to depend upon whether the process can compete with boneblack refining on the basis of cost and sugar yield and upon whether inversion of sugar can be held down to an economic limit. There are, however, one or two small inland refineries which utilize ion exchange in the refining of raw cane sugar for the production of liquid sugars (sugar sirups). The presence of some invert sugar in such products is generally not objectionable, in fact a high content of invert sugar is desirable in many uses of sugar sirups.

The process of ion exchange involves the passing of the cooled, dilute sugar solution to be treated over a pair of beds, the first containing the cation resin and the second the anion resin. The resins are contained in cylindrical, rubber-lined steel tanks, which are only about half filled with resin, to allow space for vigorous back-washing of the resins. As a rule, a treatment unit consists of four pairs of columns, which are handled in rotation through the several steps of the operating and regenerating cycles. The resins are rather coarsely granular, so that the pressure drop of liquids

percolating through them will not be excessive. They are covered with water before use, which causes considerable swelling of the particles.

The operating cycle consists of "sweetening on" (displacing the water with the sugar solution), running on "service" until the cation effluent has sharply increased in pH from an original 2 or less and the anion effluent which is originally pH 8 or higher has fallen off to about neutrality, sweetening off the resins until the effluents are about 1°Brix, "backwashing" to remove any sediment, and, finally, draining out the excess water. The resins are then ready for regeneration. Because of the large quantity of acid required (2 or 3 molar equivalents of the cations to be removed), the cation resin is regenerated in 2 or 3 stages, say, first with twice-used acid, then with once-used acid, and finally with fresh acid. For the anion resin, caustic soda is used if it is highly basic, ammonia, if the resin has a low basicity. Since the quantity of alkali required is relatively small (little more than the molar equivalent of the anions to be removed), a single-stage regeneration is usual. Ammonia, moreover, can be recovered after use. The resins are thoroughly rinsed with water to remove the regenerants, and are then ready for another operating cycle.

The application of ion exchange can scarcely be said to be permanently established in any branch of the sugar industry, and its future status has not been determined. New resins for sugar work, such as a very highly basic anion resin designed for use before the cation resin, and a mixture of cation and anion resins to be used in one bed, are being developed. The two components of the latter type must necessarily be regenerated separately and for this purpose they are separated by flotation, rendered possible by a sufficiently great difference in specific gravity. After regeneration, the two resins are again mixed for re-use.

**Extraction with Methanol.** A novel process of refining cane sugar, which has passed the pilot-plant stage, consists of extracting the whole raw sugar with hot methanol (9). By this extraction, the coating of mother liquor surrounding the sugar crystals is removed. The soluble impurities, and also a small amount of sucrose, are dissolved in the methanol, while insolubles are also carried away, as the extraction is carried out under agitation. After centrifuging and drying the washed sugar, a product testing 99.7° and of a very light brownish color is obtained. The insoluble matter carried away by the methanol is separated by sedimentation, and the methanol is distilled off from the soluble solids, leaving molasses from which a small amount of crystalline sugar, testing about 92°, separates out.

**Crystallization.** Multiple-effect evaporation of the char-filtered liquors, crystallization in vacuum pans, and spinning (purging) of the magmas in centrifuges are similar to the corresponding processes in raw sugar manufacture, except that the resulting crystals of refined granulated sugar are thoroughly washed in the centrifuges with pure water to remove the remaining mother liquor completely. Typically, four boilings for granulated sugar are performed, three on the char-filtered, washed sugar liquor and resulting sirups (mother liquors), and one on the char-filtered affination sirup, with which is mixed the sirup from the third boiling (see Fig. 2). The sirup from the fourth boiling, which is too dark to boil for recovery of granulated sugar, may be char-filtered and the resulting lemon yellow liquor used for the production of soft (brown) sugars, or it may be sent wholly or in part to the remelt department, along with any unfiltered affination sirup or thick sweetwater which is coming through at the time.

The remelt work consists of boiling these dark-colored, low-purity (about 80°)

materials, and centrifuging to obtain remelt sugars (see Fig. 2). The remelts, which are rather similar to raw sugar, are melted and refined to produce granulated sugar. The low or final remelt magmas are matured in crystallizers before spinning, just as are the final magmas in raw sugar manufacture. The sirup spun off from the final magmas, from which no more sugar can be obtained by further crystallization, is called *unfiltered refiners' sirup* or (especially if it resulted in large part from raw affination sirup), *refiners' blackstrap*. It is very dark in color and somewhat bitter in flavor. When diluted, heated, filtered through boneblack, and again boiled thick, it becomes the product known as *filtered refiners' sirup* which is an edible product, used largely by sirup blenders.

**Packaging.** The white granulated sugar from the centrifuges is dried in large, nearly horizontal, revolving cylinders called granulators, through which heated air is passed. To eliminate oversize crystals and lumps and to classify into various grain sizes, the sugar is passed through vibrating screens, after which it is run into storage bins and therefrom packed in bags or cartons, as desired. Soft (brown) sugars are not dried, but are packed as they come from the centrifuges, containing 3–4% moisture. In the manufacture of the sparkling cut tablets, the purest and whitest sugar that it is possible to obtain by a special process of crystallization is formed into large slabs, which are notched with a saw and then broken into individual tablets. By this means, the glistening crystal surfaces are preserved. Cube sugar and pressed tablets are made from pure white sugar crystallized in the usual manner and afterward formed into the desired shapes on a revolving drum containing multiple molds or pockets, followed by drying. Powdered sugars are made by grinding granulated sugar and sifting through silk or nylon cloth in revolving bolters to obtain the coarse, medium, and very fine (*confectioner's*) varieties. Much of the confectioners' grade is made in mills that grind so fine that no subsequent bolting is necessary. Modern machines that are very largely automatic are used for weighing the various grades of sugar produced, filling into packages, closing by sealing or sewing, and packing small units in multiple into outer bags or other containers. The filled packages are stored and shipped with the aid of materials-handling equipment, such as mechanical conveyors, trailer trucks hauled by a tractor, and fork-lift trucks.

The manufacture of **liquid sugar (sugar sirup)** for the food processing trade was begun about 1925 and has grown to large proportions. In this operation, the washed raw sugar liquor is defecated and decolorized and then evaporated to 67° Brix, furnishing a pure sucrose solution that is saturated at ordinary temperatures. If the sucrose has been partially or fully inverted, which is desirable for several food industries, it is evaporated to a higher density (70–76° Brix), as the invert sugar prevents crystallization at such higher densities. Some liquid sugars are made by dissolving refined white granulated sugars. Liquid sugars are shipped in tank trucks, railroad tank cars, and sometimes in tank vessels by water. Obvious advantages are the savings to the refiner by elimination of the package and packing costs and the process steps of crystallization, drying, screening, and handling of packaged sugars. Food processing plants save in the reduced cost of the product and in warehousing and handling costs, since the sirup can be cheaply pumped to all parts of the plant. Plants far distant from the producing refinery are precluded from using liquid sugar, because of the cost of freight on the water content of the sirup. These liquid sugars, however, are very perishable unless protected against surface fermentation, which can be accomplished by ultraviolet lamps in storage tanks and by efficient filtration of the air admitted.



## Beet Sugar

### CULTIVATION

The sugar beet is a white variety of the species *Beta vulgaris*. The root approximates an inverted cone in shape, with tap roots extending as much as 5 or 6 ft. into the ground. Eventually decaying there, the roots increase the soils' humus content, which, together with the deep plowing, liberal use of fertilizers, and intensive cultivation which the beet crop receives, improves the soil. It is, therefore, advantageous to rotate sugar beets with other crops, whose yields are thereby improved. Sugar beets average about 2 lb. in weight. The foliage grows to a height of about 14 in. above the ground. The average annual yield of beets in the U.S. is about 12 tons per acre and has reached as high as 25 tons in some areas. Sugar, formed by photosynthesis in the leaves, migrates to and is stored in the roots, which contain on the average about 15% of sugar. Sugar beets flourish in temperate climates. Warm, sunny days and cool nights are required, with about 16 in. of rainfall or the equivalent in irrigation, to attain a high sugar content.

The principal beet-growing regions in the U.S. are the central and northern Rocky Mountain States, California, and the region of the Great Lakes. Canada also produces a beet crop. Europe depends for its sugar supplies largely on the beet crops of France, Belgium, Germany, Czechoslovakia, and Russia. Prior to World War II, the planting, thinning, cultivation, and harvesting of sugar beets required a vast amount of hand labor. In the U.S., much transient labor was employed for the growing season. With the advent of the war and the attendant acute labor shortage, great impetus was given to the development of labor-saving agricultural machinery, so that today the culture of beets has become mechanized to a great extent.

The production of beet seed that will furnish good yields of beets of high sugar content is conducted by specialists who work in, or under the direction of, the beet processor's agricultural department. Important assistance is rendered by the U.S. Department of Agriculture and state agricultural departments. Formerly the seed was planted in its original form as harvested, but for the last decade or so the "seed balls" have been subjected to a process whereby the outer corklike layers are removed, and the seed is reduced to a uniform size by screening and freed of objectionable matter by air separation. The number of seed germs per particle is decreased by this process, which reduces the amount of thinning of the young plants that is required.

Planting takes place in the spring in most localities, and the beets are harvested in the autumn and early winter, before there is danger of their freezing in the ground. At that time they are reasonably mature as regards sugar content. At harvest the tops are cut off either by hand or by mechanical harvester and left upon the field. It is common practise to turn cattle or sheep into the fields to feed upon the beet tops, which are excellent for the purpose. The beets are carried by motor trucks to a receiving station maintained by the processor at a railroad siding, or are trucked directly to the sugar factory if sufficiently close at hand. Beets are transported from receiving station to factory in bottom-emptying gondola cars or, in the warmer regions, as California, in special cars with slatted sides for ventilation. In a few cases, where navigable water is available, transportation is by barge (8). Beets harvested more rapidly than the factory can process them are stored in piles at the factory's beet sheds or outdoors.

Sugar beets are subject to damage during growth by numerous insect pests, certain fungi, and plant diseases. The most important malady is curly top, a disease transmitted by an insect known as the beet leafhopper. The curly top disease for a long period of time made severe inroads in the western United States. Losses from this cause have, however, been greatly reduced through the development of resistant varieties of beets (8).

### MANUFACTURE

Beet sugar factories start the processing operation each year when the beets begin to arrive and continue working after the harvesting is completed until all stored beets have been sliced. Except in California, the harvesting period may be from, say, October 1st to November 30th, while the factory campaign may continue on into January. In California, harvesting and processing are concurrent, the campaign covering about 150 days.

The processor generally pays for beets on the basis of a sliding scale in which their

sugar content and the net sales return to the processor for sugar during a specified period are factors. In the middle-western region, however, the growers usually receive for their beets about 50% of the proceeds from the sale of sugar and by-products produced therefrom.

Loads of beets arriving at factory or receiving station are first weighed (see Fig. 3).

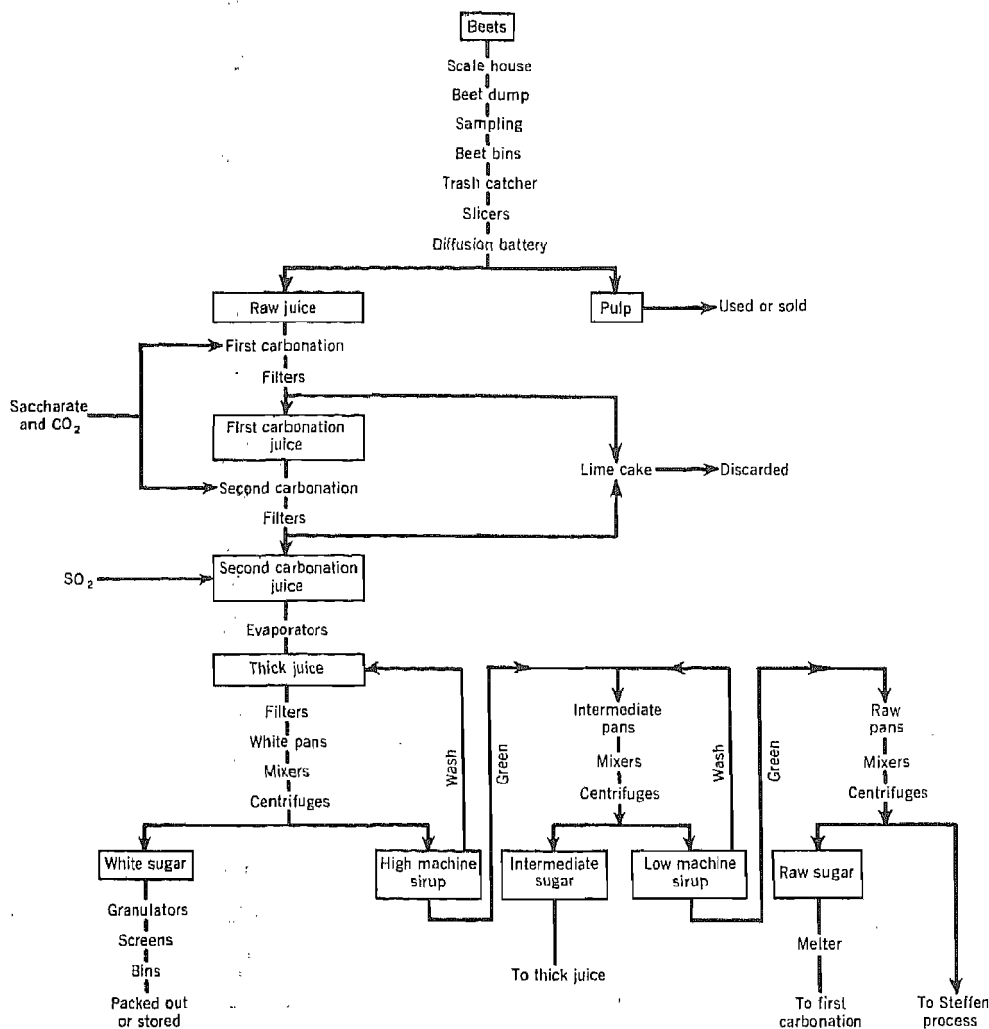


Fig. 3. Flow sheet of beet sugar manufacture.

The load is dumped, and the beets are passed over a screen which returns the loose dirt, stones, etc. to the vehicle, which is then weighed again. The difference represents the gross weight of beets delivered. The beets are next sampled, and the sampled beets are weighed, topped, and brushed to remove adhering dirt. Topping consists in cutting off the greenish top portion of the root where the leaf stalks were attached, since this crown or top is low in sugar content and high in soluble impurities, thus yielding little if any crystallizable sugar. The cleaned, topped sample is again weighed

to determine the percentage tare, which is applied to the gross weight of beets delivered, to obtain net weight. If the sugar content of the sample is to be determined, which is always necessary when payment is predicated on the sugar content of the beets of different growers, rather than the factory average sugar content of the sliced beets, its sugar content is determined.

Beets are flumed into the factory from carrier or storage pile, this being possible because their specific gravity is close to that of water. They pass through a trash catcher and a washer. The beets are then weighed on automatic scales, this weight being used in connection with the sugar content determined in the laboratory, for the calculation of factory yield of sugar. They are fed to the slicer, a rotary drum in which the beets are forced against the serrated edges of sharp knives mounted on the periphery of the drum so that the slices pass through and fall away from the drum. The slices, or cossettes, are long, slim slivers which in size and shape resemble shoe-string potatoes.

Extraction of sugar from the cossettes takes place in a battery of usually 10 or 12 diffusion cells, which are closed, cylindrical tanks arranged in either circular or linear formation, each holding about 5 tons of cossettes. Here hot water is percolated countercurrently through the series of operating cells. Sugar passes into solution from the cossettes probably in three ways: (1) from plant cells ruptured in the slicing, (2) from cells swollen and ruptured by osmosis of water through the cell walls, and (3) by dialysis of sugar through the walls of cells that are not ruptured during slicing or by swelling. Simple diffusion of the sugar in solution from a less concentrated to a more concentrated medium also plays a part. Soluble impurities of the beet are inevitably carried into solution along with the sugar, but to the least extent where true dialysis occurs, as only the crystalloids are then removed, unless the plant cells are grossly swollen (8). The solution is reheated between cells, so as to maintain its temperature at about 180°F. Usually two cells at any given time are out-of operation for emptying and refilling. Continuous diffusers have to some extent replaced the conventional battery type. The pulp (exhausted cossettes) is passed over a dewatering screen and is then either filter-pressed or stored in a wet-pulp silo. Much of the pulp produced at present is dried, in which form it can be shipped economically. Practically all beet pulp is utilized as feed for cattle.

The solution running from the last-filled cell is called diffusion juice. It contains about 10–15% of sugar, representing some 98% of the sugar contained in the sliced beets. Because of the soluble nonsugars also extracted from the beets, however, the purity of the juice is only about 85°. The diffusion juice is heated with milk of lime, or with lime saccharate if the factory is one that employs the Steffen process (see p. 221), and subjected to double carbonation. Carbonating the juice to near the neutral point in one operation gives a precipitate that is difficult to filter and causes some of the precipitate to redissolve; therefore carbonation is carried out in two stages. The limed juice is first gassed by bubbling carbon dioxide through it until the optimum point of alkalinity and filterability is reached. It is then filtered, after which the carbonation is finished in a second stage and the juice is again filtered. In some factories a part of the lime added before the first carbonation is added gradually in a pre-defecation step; this treatment is said to achieve a more complete coagulation of colloidal substances which would subsequently retard the crystallization of sugar. Carbonation takes place in tanks sufficiently tall to allow considerable space for foaming above a height of 6 ft. or more of juice. The older, conventional batch system of

carbonation is still in wide use, but continuous carbonation is also widely used in the U.S. (8). In continuous carbonation systems, a tray-type thickener is used to separate the heavy first-carbonation precipitate, followed by filtration of the sludge so collected. The filtrate obtained after the second carbonation is given a mild treatment with sulfur dioxide (sulfitation) to lighten its color and is sometimes boiled to break up bicarbonates. It may or may not be filtered to remove any slight precipitate thus formed. The purified juice is called thin juice.

The large quantities of lime required in the processing of beets are obtained by burning limestone mixed with coke, usually in Belgium-type kilns. Strontium hydroxide has been used in some European sugar refining. The operation also supplies the carbon dioxide for carbonation of the juice. Sulfur dioxide for sulfitation is generated by burning sulfur or, in some localities where it is obtainable at sufficiently low cost, liquid sulfur dioxide is used.

Just as in the refining of cane sugar, boneblack is the principal agent for purifying the sugar solution before crystallization, so in the manufacture of beet sugar, purification is achieved principally by carbonation. Mineral substances that form insoluble carbonates are removed in that form, phosphates and other inorganic bodies are precipitated, colloids, including coloring matter, are coagulated, and other organic substances are removed by occlusion in the voluminous precipitate of calcium carbonate. Additional removal of colloids and further decolorization are frequently achieved by the application of activated carbons, sometimes at the carbonation or sulfitation stage and sometimes after evaporation of the juice. The spent carbon in any case is removed in one of the regular filtration operations which would be conducted whether or not carbon were used. In most cases, there is no attempt to regenerate the carbon. Filter aids, principally diatomite, are also used to a considerable extent in the several filtrations. The relatively new process of purification by ion exchange (see p. 214) has been given quite extensive study and practical application in the beet sugar industry. Large installations on full factory scale have been made in at least three factories and operated for considerable periods of time. The process appears to have at least as good a chance of ultimate survival for beet sugar as for cane sugar.

The thin juice is evaporated in multiple-effect evaporators to about 60° Brix or higher, the concentrate being known as thick juice. Intermediate sugar from the second boiling and occasionally even "raw sugar" from the third boiling (see below), is melted in the thick juice and the resulting mixture, called standard liquor, is the material used for boiling white sugar. It is usually filtered (always, if treated with carbon) and sometimes even refiltered, before going to the vacuum pans. Only one boiling of white sugar can be made, as the sirup spun off from the first crop of crystals is not sufficiently free from color and other impurities to permit of further production of white sugar. Two remelt boilings, called respectively, intermediate and raw strikes, are made. As before stated, the intermediate sugar, and in some cases the raw sugar, is melted in thick juice to form the standard liquor for the white sugar pan. Usually, however, raw sugar, which is naturally of low purity, is melted in sweetwater and mixed with diffusion juice before the first carbonation.

In many factories, in the white sugar strike and the intermediate sugar strike (see Fig. 3) the wash liquor is kept separate from the original centrifugate or "green" fraction. In the white sugar strike, the wash fraction goes to the thick juice for processing into white sugar, while the green fraction goes to the intermediate pans for separation of the intermediate strike. In the intermediate strike, the wash fraction

is recycled and mixed with the green fraction from the white strike for boiling intermediate strikes. The green fraction is used for boiling raw strikes. Where sirup separation is not practiced, the whole intermediate sirup goes directly to the raw pans. The crystal magma from raw strikes is matured in crystallizers for about 72 hours and then centrifuged. The final sirup so obtained is called molasses. It may be sold without further processing for use in cattle feeding or in the manufacture of yeast, but in very many cases it is subjected to the Steffen process for the further recovery of sugar.

In the **Steffen process** the molasses is diluted, cooled to a low temperature (not exceeding 18°C.), and treated with finely pulverized lime (CaO) under vigorous agitation. The weight of lime used is generally somewhat greater than that of the sugar present. The sugar and lime combine to form an insoluble saccharate, which is filtered off. The filtrate is heated, causing another insoluble saccharate to be precipitated. This is likewise filtered off and joins the cold saccharate, to be made into a thin slurry with sweetwater. This slurry, called saccharate milk, is used instead of milk of lime to treat the diffusion juice. During carbonation the saccharate is decomposed with the liberation of sucrose and the formation of calcium carbonate.

A typical analysis of beet molasses is: sucrose 50%; invert sugar 1%; water 17%; ash 12%; organic nonsugars 19%. It will be seen that the purity of this molasses  $50/(100 - 17)$  is about 60°. The purity of the saccharate cake is determined by carbonating a sample, filtering off the precipitate or calcium carbonate, and testing the filtrate for purity. This saccharate purity is about 95°, which shows that the Steffen process is well worth while. After a time, however, the recycling of impurities by returning the saccharate to process results in a gradual deterioration of the quality of the molasses produced, which makes it impossible to obtain saccharate cake of sufficiently high purity. Molasses is therefore periodically discarded. Raffinose is a particularly troublesome impurity, since it combines with lime to form an insoluble, saccharatelike compound, which reverts again to raffinose when the diffusion juice is carbonated. If allowed to accumulate in the factory to a considerable concentration, raffinose not only lowers the purity of the saccharate cake, but affects the appearance of the refined sugar produced. Sugar crystals boiled from a liquor containing any considerable amount of raffinose are elongated even though not containing much raffinose. The Steffen filtrate (waste water) is either discarded or concentrated for the manufacture of monosodium glutamate. Factories that employ the Steffen process are called Steffen houses; those that do not are known as straight houses.

In one factory in the U.S., at Johnstown, Colorado, discard molasses from Steffen houses is processed for further sugar recovery, by a barium hydroxide treatment, which has the advantage of forming a saccharate of very low solubility, without precipitating raffinose and other carbohydrates. Thus, a saccharate of high purity is obtained, even from discard molasses. Barium hydroxide for the process is obtained by calcining witherite (barium carbonate) with silica in the form of sand in a rotary kiln. Barium hydroxide is leached out from the clinker with hot water. Subsequent losses of barium in the process are made up with barite (barium sulfate) rather than witherite. The molasses is diluted, the barium hydroxide solution is added, and the saccharate is filtered off, slurried, and carbonated to liberate the sucrose. Filtration of the resulting solution, which now carries barium carbonate in suspension, furnishes a sugar solution of about 95° purity, from which white sugar is obtained by processing it much as in the refining of raw cane sugar including a filtration through boneblack. The barium carbonate filter cake is regenerated, that is, reconverted to the hydroxide, by calcining with silica and leaching out as already described.

The granulated sugar produced in beet sugar factories is dried, screened, and bagged, the equipment being similar to that employed in cane sugar refineries. Some powdered sugar is manufactured, but the beet sugar process does not ordinarily furnish the water-white liquor that is required for the production of cube and tablet sugars, or the extra white, coarse-grained specialties that most cane sugar refineries turn out. Neither can beet sugar liquor, because of color, odor, and flavor, be used for the manufacture of liquid sugar or soft sugars. Some soft (brown) sugar is made by impregnating finely grained beet sugar with a cane sugar molasses (refiners' sirup) in the centrifuges. Beet granulated sugars are dissolved to make liquid sugars.

Beet sugar processing equipment such as filters, vacuum pans, centrifuges, granulators, and screens is similar to that found in cane sugar refineries, with the exception that rotary vacuum filters are employed in modern installations to a much greater extent than in the cane sugar refineries. Granulated beet sugar as manufactured in the U.S. is for practical purposes identical with refined cane sugar. In the past a rather widespread prejudice that arose against beet sugar was caused by the fact that in the earlier days of the beet sugar industry much of the product turned out was not properly processed and therefore was not thoroughly freed from potassium salts and organic impurities.

In Europe it was customary to manufacture raw beet sugar in factories conveniently located with respect to the beet fields and then to send the raw sugar to a centrally located refinery for processing into white or refined sugar. This practice still persists in some localities. Boneblack is employed and the operation is very similar to cane sugar refining. Also, cane sugar refineries in England and on the European continent process considerable quantities of raw beet sugar, sometimes in actual mixture with raw cane sugar.

### Control

The sugar industry was one of the first to adopt systematic control of processes by means of chemical and physical tests. As we have seen, the sugar content of beets purchased by the processor is in most cases a factor in the price paid, while the cane sugar refiners invariably pay for their raw product on the basis of its weight and polarization. In some countries, sugar content of cane is a factor in fixing its price. In the manufacture of raw cane sugar, as well as in refining and beet processing, an accurate determination of the quantities of sucrose entering and in the products and by-products turned out is necessary for the calculation of the loss of sucrose sustained, or conversely, the yield of sugar obtained, over a given period of time. In the cane sugar refining industry an account is kept also of the nonsucrose constituents of the input and output, which are invert sugar, water, insolubles, soluble ash, and organic non-sugars.

At stated intervals a careful inventory of all materials in process is taken, in which the contents of all tanks, crystallizers, bins, etc., are determined by outage measurements or other means. A representative sample of each item is taken and sent to the laboratory for analysis. Density and either purity or full analysis are determined. From these data the pounds solids and pounds sucrose or pounds of each constituent in the inventory (stock in process) are calculated. The total weight in pounds of sucrose in the raw material that entered the process during the period, plus the weight of sucrose in process at the close of the period, is the net input. Sub-

traction therefrom of the total weight of sucrose in all products and by-products turned out during the working period gives weight in pounds of sucrose lost in processing. All white sugars are considered to be 100% sucrose.

In the manufacture of beet and raw cane sugar it is customary to show separately on a consolidated yield statement the known losses, as in the cane bagasse, the beet pulp, and the press cakes, and to report the remainder (inversion, entrainment, fermentation, etc.) as unknown losses. It is also customary to report the sugar lost in the molasses, although this is obviously not a disappearance or destruction of sucrose, but a conversion from crystallizable to uncrystallizable form. In cane sugar refineries, attention is focused mainly on the total loss of sucrose in the refining process, expressed as percentage by weight of the raw sugar melted, and expressed as "granulated yield," which may be -1%, or -2%; it is calculated from the total quantity of 100% sugars (granulated, powdered, etc.) produced, and from the quantity of 100% sugars that the melt, according to its composition, would be expected to yield. When soft sugars are produced, since they contain less than 100% of sucrose, their granulated equivalent is calculated by a suitable formula and added to the 100% sugars actually produced. Formulas for expected or theoretical yield differ somewhat among the various refiners. With a theoretical yield from the raw sugar based on the proportion of its sucrose content that would be carried into the final molasses by its content of solid nonsugars, if none of the nonsugars were removed, it is possible to have a plus granulated yield. This is because the boneblack removes by adsorption a considerable proportion of the nonsugars contained in the melt, thus releasing an appreciable quantity of sucrose for crystallization.

The loss of sucrose in a properly operated refinery is only a fraction of 1%. Loss or gain of invert sugar is important to know, as it indicates excessive inversion of sucrose, if such has occurred in the process. Normally, there is a loss of invert sugar. There can be no doubt that a small amount of sucrose is inverted here or there in the process, which would show as a gain in invert sugar on the yield statement. Invert sugar, however, particularly the levulose component, is constantly being destroyed by heat in the slightly alkaline liquors and is possibly adsorbed to some extent by the boneblack. The result is usually a net loss of invert sugar. There should always be a substantial loss of ash in refining since that constituent is extensively adsorbed by the boneblack and later removed from the process in the waste wash water from the char filters.

In all three branches of the sugar industry each step of the process, as well as the quality of the products, is controlled by physical and chemical tests made partly in the plant laboratory and partly at various process stations in the plant. The solids content of liquids is gauged by Brix hydrometer or by refractometer. Apparent purity, that is, the percentage of sucrose determined by direct polarization in the solids as determined by hydrometer or refractometer, is one of the tests most frequently made throughout the process. Another is effective alkalinity or acidity expressed as pH, for which the colorimetric method and electric pH meters are commonly used. Both pH tests and the determination of absolute or total alkalinity by titration, expressed as grams NaOH or CaO required to neutralize 10 ml. of juice (phenolphthalein indicator), are used in controlling liming and carbonation in cane and beet sugar factories. Both visual and spectrophotometric methods for the determination of color are extensively employed on liquors and final products, especially where white or refined sugar is concerned. Very careful control is exercised at all points where sugar

may be lost unwittingly or in more than a necessary minimum quantity, as in cane bagasse or beet pulp, press cakes, vacuum-pan and evaporator vapors and condensates (by entrainment), and (in refineries) the effluent of char filters when being turned to waste. The purity of the final molasses must, of course, be controlled by frequent tests to assist in keeping it as low as possible.

Bacteriological control of mesophilic organisms usually consists simply of making sure that no dilute material is allowed to remain longer than necessary at a temperature lower than about 70°C. If the temperature drops much below that the solution may ferment rapidly with destruction of sucrose. Tests are made as needed, especially for yeasts and molds in refined products. Thermophilic bacteria, however, survive the high and sustained temperatures of sugar manufacture and refining and actually propagate at temperatures considerably higher than 55°C., which is their optimum temperature. The spores of such organisms pass into the refined sugar and have been found to be a cause of spoilage in canned, nonacid vegetables. Control consists of making routine counts of thermophiles in the product and, when necessary, testing materials in process to detect sources of these bacteria. Many producers furnish granulated sugar guaranteed to meet standards set by the National Canners Association Research Laboratories, testing each lot of such sugar produced to assure compliance.

Process control by instrumentation in the sugar industry has made much progress in the last two or three decades. Recording thermometers, as well as indicating and recording pyrometers (on kilns), are in general use. Instrument control of sugar boiling, generally by regulating the degree of supersaturation through what is known as boiling point rise (b.p.r.) or elevation (b.p.e.) is widely practised. The degree of supersaturation may also be measured directly. Other methods employ refractometers or depend upon the electrical conductivity of the boiling mass or on vapor pressure measurements. Automatic liming through pH control has found application in the defecation of cane juice and elsewhere in the sugar industry. Many other controls by instrumentation may be found in sugar factories and refineries.

### Uses and Grades

By far the largest use of sugar is for sweetening or otherwise conditioning foods, including beverages, in the household and in the food industries. There are, however, some nonfood uses for sugar, of which the manufacture of tobacco (*q.v.*) products is a leading one. Here an important use is as a humectant. Sugar also has been used in the manufacture of explosives, and certain products of microbiological origin, such as citric acid, penicillin, and the plasma extender, dextran. These industrial processes, however, consume a relatively small quantity of sugar in the aggregate. Most citric acid is made from molasses. Through research and development the sugar industry is striving to increase the use of sugar for nonfood industrial purposes.

The use of sugar in the food industries is in bakery processes (*q.v.*), carbonated beverages (*q.v.*), confectionery (*q.v.*), and chocolate (*q.v.*), flavoring and table sirups, ice creams, cake and pudding mixes, and preserves, jams, and jellies. Sugar is also used in the curing of meat (*q.v.*) and in the preparation of mince meat, baked beans, and pickles, to name a few of many other food uses.

The grades of sugar used in food processing are: *granulated*, which comes in a



number of particle sizes, ranging from very fine to the coarse crystals used largely for decorative purposes; *powdered*, of extremely fine particle size, used largely for cold icings and cake fillings, and coarser grades for coating doughnuts and the like; *soft or brown sugars*, used in many dark and medium-colored products, especially baked goods, (brown sugars are extremely fine crystals of sugar, covered with a film of purified, dark colored sirup; of 15 grades, ranging from light to dark brown, numbers 6, 8, 10, and 13 are used by food manufacturers); *turbinados* (partially refined), used in replacement of granulated sugar for reasons of economy where the sugar need not be white; *liquid sugar*, used in replacement of granulated wherever its water content is desirable or can be compensated for by reducing water used in the formula or elimination of water by boiling. The invert types of liquid sugar have their special uses in various food industries.

Selection of sugars for household use should be: *granulated* (fine or extra fine) for general cooking, baking, and candymaking, *light brown* (grade no. 8), if preferred, for sweetening cereals and some fruits, and also in baking where its flavor is desired and the color permissible; *dark brown* (grade no. 13) for sweetening dark-colored foods such as gingerbread and baked beans (the flavor of brown sugar is distinctly different from that of the raw sugar by-product, molasses, because of the additional processing it has received in the refinery); *confectioners' powdered* (extremely fine) for uncooked icings and fondants; *coarse powdered* or an ultrafine granulated sugar for sweetening fruits, cereals, and iced beverages (dissolves more readily than confectioners' sugar at low temperatures); *lump sugar* in cube or tablet form for hot beverages.

There has been much misconception regarding the role of sugar in the human diet, both quantitatively and qualitatively. During World War II, several nutritionists recommended that 175 lb. of sugar per capita per year be earmarked for the U.S. Armed Forces. This contrasts with a total annual per capita consumption of sugar between 90 and 100 lb. in the U.S. (16). Refined sugar (both white and brown) is among the most nutritious and least costly per calorie of all carbohydrate foods. Raw sugar is not intended for direct consumption as a food and should not be so used, as it may contain sand, dirt, bag fibers, harmful bacteria, or other objectionable matter. Refined brown sugars contain decidedly more minerals than raw sugar and are clean and sanitary. The value of balancing by the addition of sugar, a diet that falls below recognized recommendations for caloric intake has been demonstrated (7,14,17). The relationship of sugar to dental caries has recently been the subject of intensive scientific research. Evidence has been presented to suggest that tooth decay can best be combated by a properly balanced diet (14,17) of the mother and of the child during the period of tooth development.

### Legislative and Economic Aspects

During World War I, the loss of beet sugar output in the battle areas of Europe was gradually compensated for by expansion of cane sugar production, particularly in Cuba and Java. Subsequent recovery of the European sugar beet industry brought about a disastrous overproduction. In 1933, Cuban raw sugars sold in New York for 0.57¢ per pound, an all-time record low.

To meet this situation, twenty-one sugar-producing countries signed, in 1937, an "International Sugar Agreement," under which exporting countries agreed to control production and to sell only fixed quotas in the world market.

This London Agreement benefited the industry during the few years in which it operated effectively. During World War II, it was again suspended while conditions were disrupted by hostilities. After a period of recovery, and when the threat of over-production again appeared, a similar new International Agreement was concluded in London on August 24, 1953.

Before 1934 the sugar industries of the mainland United States and insular possessions were protected by high tariff duties. Expansion of production, threatening oversupply, led to adoption of a quota system for the United States market through the Jones-Costigan Amendment to the Agricultural Adjustment Act of 1934. Subsequent laws have somewhat modified details but have maintained the quota system, benefit payments to growers for "soil conservation," and an excise tax payable into the Treasury.

The quotas of Hawaiian, Puerto Rican, Virgin Island, Philippine, mainland cane, and domestic beet sugars that may be marketed within the United States are fixed by law. The quotas for Cuba and other foreign countries are based upon a consumption estimate made by the Secretary of Agriculture each year in advance. Revised estimates of consumption may be made during the year with consequent adjustment of foreign quotas. Reallocations are also made to meet deficiencies in production in any area.

Quotas announced for 1953 were as follows (short tons, raw value):

Domestic Beet	1,800,000
Mainland Cane	500,000
Hawaii	1,052,000
Puerto Rico	1,180,000
Virgin Islands	12,000
Philippines	974,000
Cuba	2,286,720
Other foreign	95,280
Total	7,800,000

Under the quota system, tariffs have been progressively reduced to 0.625¢ per pound on full-duty raws and 0.50¢ on Cuban.

TABLE I. World Sugar Production.

Year	Production Cane Sugar (Long tons)	Production Beet Sugar (Long tons)	Production Total Sugar (Long tons)	Percentage of Cane Sugar
1885-86 <sup>a</sup>	4,289,300	2,229,973	6,519,273	65.8%
1896-97 <sup>a</sup>	5,091,857	4,954,032	10,045,889	50.7
1903-04	6,838,931	6,820,204	13,659,135	50.1
1913-14 <sup>a</sup>	9,801,536	8,634,942	18,436,478	53.2
1917-18	12,365,569	5,015,262	17,380,831	71.1
1919-20	12,227,125	3,273,798	15,500,923	78.9
1924-25	15,895,336	8,093,453	23,988,789	66.2
1929-30	17,633,924	9,175,319	26,809,243	65.8
1934-35	15,526,269	9,530,585	25,056,854	62.0
1939-40	19,330,205	11,115,917	30,446,122	59.5
1945-46	16,528,990	5,502,173	22,031,163	75.0
1948-49	21,228,706	10,312,581	31,541,287	67.3
1951-52	25,511,290	13,155,313	38,666,603	66.0

<sup>a</sup> Includes estimated production of India, not reported for these 3 years.

The 1947 Census of Manufactures showed the following figures for the sugar industry of the United States.

	Raw Cane Sugar Factories	Cane Sugar Refineries	Beet Sugar Factories
Number of establishments	82	25	74
Total number of employees	4,635*	17,376	13,412*
Value of products	\$60,135,000.00	\$818,430,000.00	\$262,872,000.00

\* Short season labor, for three to five months in many cases.

World consumption of sucrose in 1953-54 was estimated at 43,870 thousand short tons. The nearest competitors of sucrose were glucose, maltose, and lactose, at about 450, 81, and 20 thousand short tons respectively (1952). The world production of cane and beet sugars for a number of illustrative years is shown in Table I (18). A breakdown, by industries, of the consumption in 1951 is presented in Table II (16a).

TABLE II. United States Consumption of Sugar by Industry.

Industry	Cwt/1951
Bakery, cereal and allied	12,444,449
Confectionary	12,450,059
Ice cream and dairy products	5,140,380
Beverages	14,404,373
Remaining industrial food uses	15,090,833
Non-food products	793,859
Institution, home use and other	77,555,216
<i>Total</i>	138,879,168

### Bibliography

- (1) Adams, B. A., and Holmes, E. C., *J. Soc. Chem. Ind.*, **54**, 1-6 (1935).
- (2) Barrett, E. P., Brown, J. M., and Oleck, S. M., *Ind. Eng. Chem.*, **43**, 639-54 (1951).
- (3) Deerr, N., *History of Sugar*, Chapman & Hall, London, 1949, p. 13.
- (4) Hockett, R. C., *Sugar in Public Health* (pamphlet), American Public Health Association, St. Louis, 1950, pp. 23-24.
- (5) Honig, P., ed., *Principles of Sugar Technology*, Elsevier, Houston, 1953.
- (6) Lyle, O., *Technology for Sugar Refinery Workers*, Chapman & Hall, London, 1941, pp. 254-56.
- (7) Mack, P. B., *A Study of Sugar in the Diet of Children on a Sub-Marginal Caloric Intake* (Pamphlet), Pennsylvania State College, 1951, pp. 31-33.
- (7a) Mayo, E. W., Jr., *Sugar Reference Book*, Vol. 21, *Sugar* (Periodical), N.Y., 1953.
- (8) McGinnis, R. A. (ed.), *Beet Sugar Technology*, Reinhold, N.Y., 1951, pp. 74, 82, 144, 289-310, and ch. 8 and 9.
- (9) Othmer, D. F., and Luley, A. H., *Sugar*, **44**, No. 6, 1949.
- (10) Paine, H. S., Keane, J. C., and McCalip, M. A., *Ind. Eng. Chem.*, **20**, 262 (1928).
- (11) Payne, J. H., Kortschak, H. P., and Gill, R. F., *Ind. Eng. Chem.*, **44**, 1415-21 (1952).
- (12) "Purification of Sugar Juices" (Symposium), *Ind. Eng. Chem.*, **43**, 603 (1951).
- (13) Shearon, W. H., Jr., Louviere, N. H., and Laperouse, R. M., "Cane Sugar Refining," *Ind. Eng. Chem.*, **43**, 552 (1951).
- (14) Sognaes, R. F., *J. Am. Dental Assoc.*, **37**, 676 (1948).
- (15) Spencer, G. L., and Meade, G. P., *Cane Sugar Handbook*, 8th ed., Wiley, N.Y., 1945, pp. 1, 10-11.
- (16) Sugar Information, Inc., *Sugar As a Food* (pamphlet), N.Y., 1951, p. 17.
- (17) *Symposium on Dental Caries* (a supplement to *J. Cal. State Dental Assoc.*), **26**, No. 3 (1950).
- (18) Willett & Gray's *Weekly Statistical Sugar Trade J.*, *Annual Statistics* (usually appear in 2nd number of each year).

L. A. WILLS

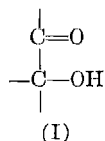
SUGAR OF LEAD. See "Lead acetate" under *Lead compounds*, Vol. 8, p. 268.

## SUGARS AND SUGAR DERIVATIVES

Survey.....	p. 228	Sucrose.....	p. 247
Occurrence.....	235	Bibliography.....	250
Physical and Chemical Properties.....	235	Invert sugar.....	251
Synthesis.....	242	Bibliography.....	256
Bibliography.....	243	D-Fructose.....	256
Commercial Sugars.....	244	Bibliography.....	261
Lactose.....	244	Derivatives.....	261
Maltose.....	246	Bibliography.....	270

## SURVEY

The term "sugar" may give rise to some confusion because it is the common name for a specific chemical compound, *sucrose*, as well as the class name for many compounds related to sucrose. Sugars (or *glycoses*) comprise the simpler carbohydrates (*q.v.*). They are characterized chemically by an "ose group" (I), composed of two car-



bons, one bearing a hydroxyl and the other an aldehyde or ketone (but not carboxyl) carbonyl or a group giving a carbonyl on hydrolysis. In general, sugars have similar properties, being more or less sweet, water-soluble, colorless substances which char when heated.

The word *saccharide* is sometimes employed as a synonym for carbohydrate or sugar. Simple or uncombined sugars may be called *monosaccharides*. Combined, they form *di-* and *trisaccharides*, etc. Polymers of two to about nine sugar units are called *oligosaccharides*. If the molecule contains many more sugar units, it is called a *polysaccharide* (*q.v.*).

Free and combined sugars occur throughout the plant and animal kingdoms. This is evidence of their importance. For example, sucrose is the product of the photosynthetic fixation of solar energy. As sucrose, this energy is transported throughout the plant, and in some plants it is a form in which energy is stored. Sugars are the building blocks that make up the polysaccharides starch (*q.v.*) (glucose), inulin (fructose), and mannan (mannose). These polysaccharides are examples of common energy-storage substances in plants. Animals make temporary storage of energy as the glucose residues in glycogen. Built into cellulose (*q.v.*), pectin (see *Pectic substances*), and xylan, sugars contribute to the structural strength of plants. Insects and crustacea rely on chitin built up from D-glucosamine for skeletal protection. The roles of other sugars are less well understood. They are of both physiological and economic importance for they appear in compounds relating to such diversified functions as immunity to disease, blood types, and cardiac stimulants.

## CLASSIFICATION, NOMENCLATURE, AND FORMULAS

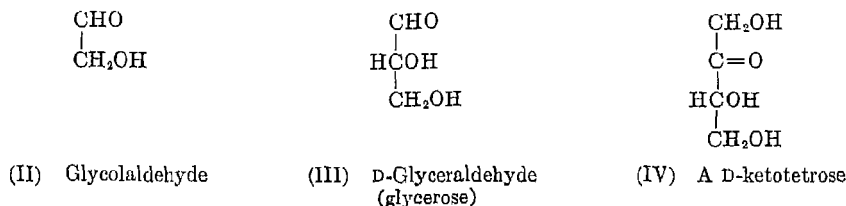
Comprehensive rules of carbohydrate nomenclature have been published (1).

Sugars may be classified in several ways, among which are: nature of the car-

bonyl group (*aldoses* and *ketoses*), length of the carbon chain (*trioses*, *tetroses*, *pentoses*, *hexoses*, *heptoses*, etc.), and changes in structure (*deoxy-*, *amino-*, *anhydro-*, etc. sugars), as well as the degree of polymerization (mono-, di-, etc. saccharides).

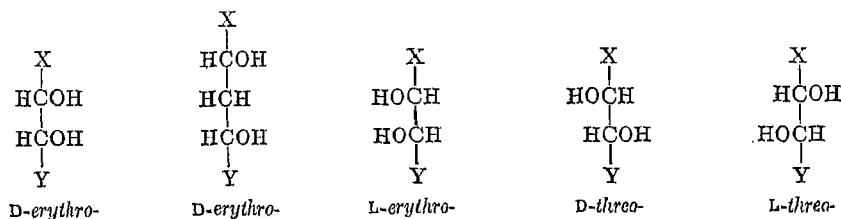
In an aldose, the carbon bearing the aldehyde group is always designated C(1); in a ketose, the carbonyl group carbon always has the lowest possible number. 2-Ketoses may be named by means of the suffix *-uloses*; before this will be a prefix indicating the number of carbon atoms in the chain, which in turn, will be preceded by the prefix denoting the configuration of the group of asymmetric centers present (see below). Thus an alternate name for D-fructose is D-arabino-hexulose.

Although the generic formulas of the simple typical sugars can be expressed quite simply as  $(CH_2O)_n$ , their structure is complex because of the stereochemistry involved (see *Carbohydrates; Stereochemistry (organic)*). Glycolaldehyde (II) should be considered the simplest sugar, but like so many of the first members of a homologous series, it is atypical. Hence, glyceraldehyde (shown as the D-form in III) is the prototype of the aldoses, and a ketotetrose such as (IV) of the ketose series. Sugars can be considered to be built up from the prototypes by inserting hydroxymethylene groups ( $-CHOH-$ ) into the chain.

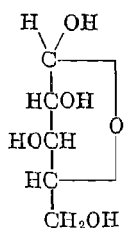
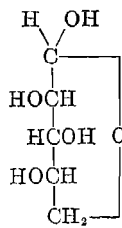


As a result of the presence of asymmetric centers, two series of sugars (D- and L-) are known. By convention a sugar structure belongs to the D-series if, with the carbonyl group drawn upward (in a projection formula), the hydroxyl group on the lowest (that is, the highest-numbered) asymmetric carbon is on the right-hand side of the molecule (as in D-glyceraldehyde (III), the configurational reference standard), and to the L-series when it is on the left. It must be emphasized that there is no relation between the configuration and the direction of rotation of the plane of plane-polarized light. For example, while D-glucose is dextrorotatory, D-fructose is levorotatory. The D- or L- in a name signifies configuration only. The direction of the optical rotation may be indicated by *dextro* or *levo*, or + or -, for example, D(*levo*)-fructose or D(-)-fructose.

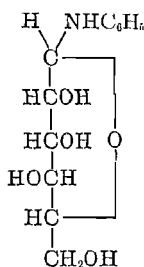
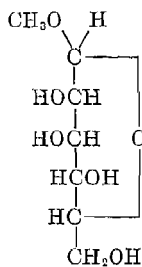
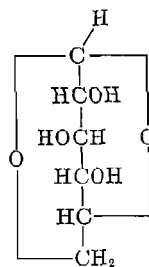
A series of asymmetric carbon atoms (not necessarily adjacent to one another) within a molecule can be indicated by an italicized prefix, derived by omitting the last two letters from the name of the aldose having the same configuration as the group in question (exceptions established by usage are *arabo* for *arabino* and *gala* for *galacto*). Thus:



The acyclic forms of aldoses or ketoses may be designated by the prefix *aldehydo* or *keto*, respectively. In the cyclic hemiacetal forms (see p. 236), the size of the ring is indicated by replacing, in the sugar name, the final -se by -furanose for the 5-atom ring (as V) and -pyranose for the 6-atom ring (as VI). In either type, the new pair of isomers resulting from the creation of a new point of symmetry are called *anomers* and differentiated as  $\alpha$ - and  $\beta$ -. By convention, if the hydrogen on the anomeric carbon (the hemiacetal carbon) is on the same side as the hydroxyl on the highest-numbered asymmetric carbon in the chain, the sugar is the  $\beta$ -form (VI). If it is on the opposite side, the sugar is the  $\alpha$ -form (V). If the hemiacetal hydroxyl is replaced, the product is a *glycosyl* (glycofuranosyl or glycopyranosyl) derivative, for example a glycosylamine (VII). If only the hydrogen of the hydroxyl is

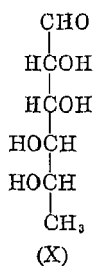
(V)  $\alpha$ -D-Xylofuranose(VI)  $\beta$ -L-Xylopyranose

replaced, the compound is a *glycoside* (as VIII). As a special case, an inner glycosidic bond may form with one of the hydroxyls of the chain to produce a *glycosan* or *anhydro sugar* (as IX, 1,6-anhydro- $\beta$ -D-glucopyranose).

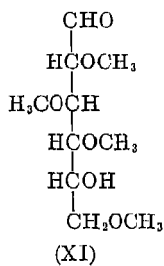
(VII) *N*- $\alpha$ -D-Galactopyranosyl-aniline(VIII) Methyl  $\beta$ -D-mannopyranoside

(IX) Levoglucosan

If an alcoholic hydroxyl group is replaced by hydrogen, this is indicated by X-deoxy- (formerly X-desoxy-, X denoting the numerical position) preceding the name; for example, L-rhamnose (X) is 6-deoxy-L-mannose (one of the "methylpentoses"). If further substitution takes place on the same carbon atom, this is indicated as in the following example, 2-chloro-2-deoxy-D-glucose. On the other hand, if only the hydrogen of the hydroxyl is substituted, this is indicated by an *O*- preceding the substituting prefix, for example 2,3,4,6-tetra-*O*-methyl-D-glucose (XI).



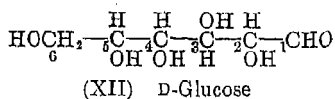
(X)



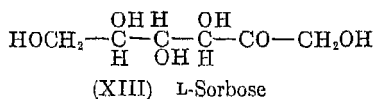
(XI)

**Methods of Writing Sugar Formulas.** There are several ways in which the formula for a sugar molecule may be written.

**Projection Formulas.** Projection formulas may be shown either vertically (Fischer convention) (see p. 231) or horizontally. When they are drawn horizontally, the carbonyl group carbon lies to the extreme right. When the hydroxyl on the highest-numbered asymmetric carbon is pointed downward, the sugar belongs to the D-series (XII) and when pointed upward to the L-series (XIII).

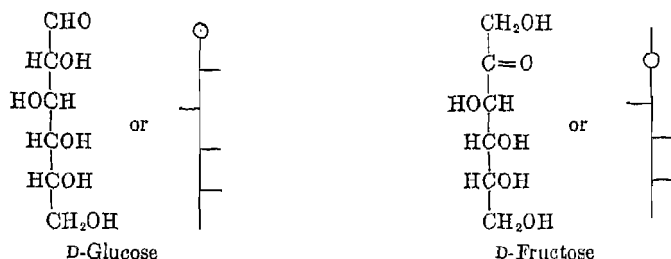


(XII) D-Glucose



(XIII) L-Sorbose

*Rosanoff Formulas.* To simplify depiction of isomeric sugars, Rosanoff invented a shorthand system shown in slightly modified form below:

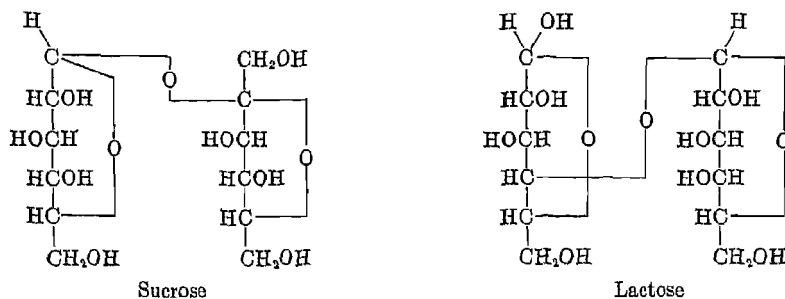


The carbon skeleton is shown as a vertical line with the position of the carbonyl carbon indicated by an O. The primary hydroxyl group ( $-\text{CH}_2\text{OH}$ ) is at the bottom of the chain (no special indication) and the intermediate hydroxyl groups are shown by a short line to the right or the left of the vertical line.

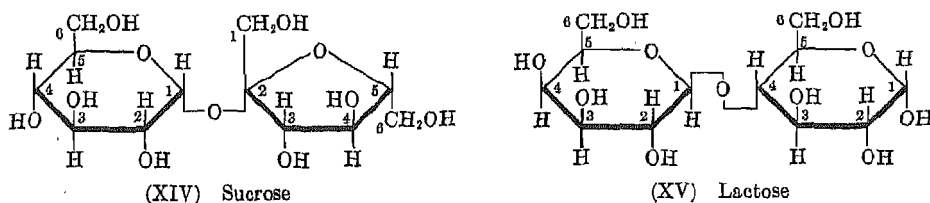
*Perspective Formulas.* An alternate way of showing sugar structure, usually attributed to Haworth, has the advantage that the spatial relationships are somewhat more realistic. A comparison with the Fischer system is made in showing the structures of sucrose and  $\alpha$ -lactose in Scheme 1.

#### SCHEME 1

##### Projection formulas



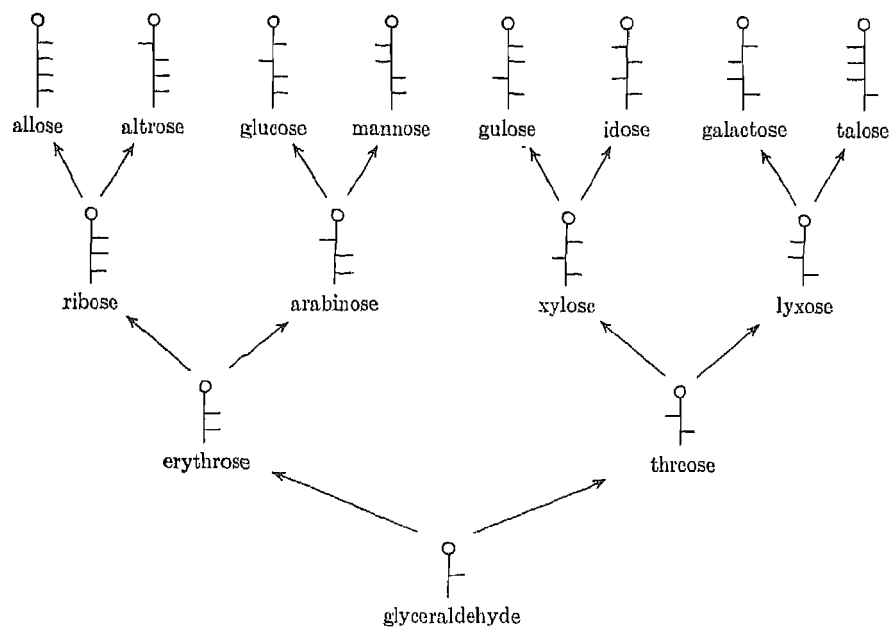
##### Perspective formulas



By convention the reducing group or lowest-numbered carbon is at the right and the  $-\text{CH}_2\text{OH}$  group with the highest-numbered carbon is written above the plane for the D-monosaccharides, but for the higher saccharides, the plane of at least one sugar unit (as the D-fructose portion in sucrose) may be inverted for convenience. Thus in showing the perspective formula for  $\beta$ -D-fructofuranose in connection with sucrose the reversed or "inverted" formula is often used (compare the formulas under "Invert sugar" and "D-Fructose").

Expansion of the D-series of aldoses and ketoses is shown in Rosanoff shorthand in Schemes 2 and 3. Remaining sugars are extensions, derivatives, or combinations of members of these series.

SCHEME 2



SCHEME 3

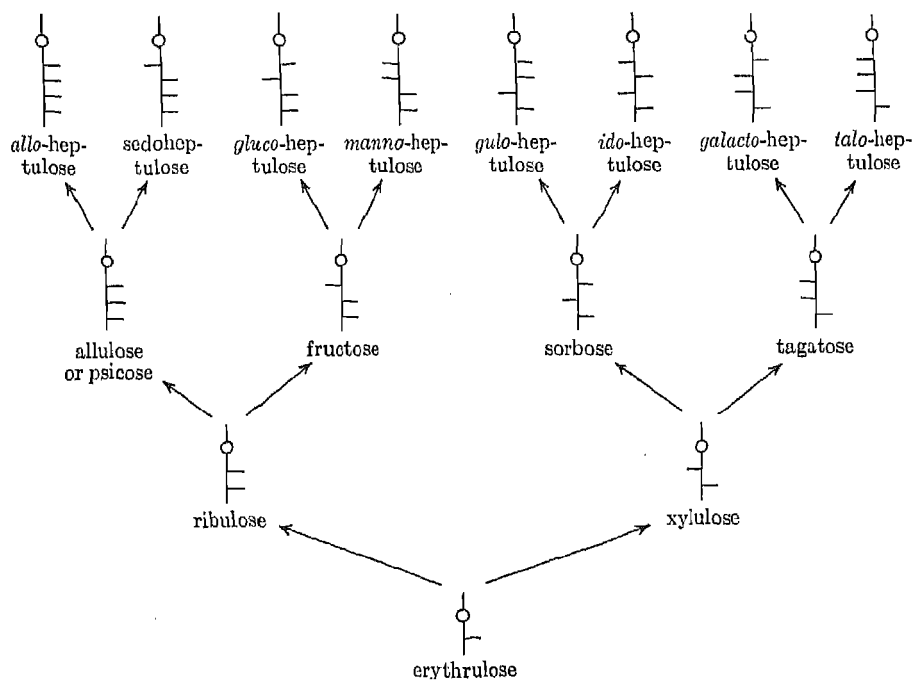




TABLE I. Occurrence of Sugars.

Name	Synonym	Source
<b>Monosaccharides</b>		
D-Glyceraldehyde	—	An intermediate in the metabolism of carbohydrates at the cellular level.
D-Ribose	—	Combined in nucleic acids of cell nuclei.
2-Deoxy-D-ribose	—	Combined in nucleic acids of cell nuclei.
D-Arabinose	—	In tubercle bacillus.
L-Arabinose	—	Combined in mesquite gum and cherry gum.
D-Xylose	—	Combined in xylans of the hemicellulose components of woody plants, corn cobs, and straw.
Apiose	3-Hydroxymethyl-L-threose	As glycoside <i>apin</i> in parsley.
D-Glucose	Dextrose	Free in fruits, honey, and blood. Combined in energy carriers, sucrose and lactose; energy storage for plants, starch, and for animals, glycogen. Structural material of plants, cellulose.
D-Mannose	—	Combined in ivory nut mannan, spruce mannan, guaran, and locust bean gum.
D-Galactose	—	Combined in lactose, melibiose, raffinose, agar, guaran, locust bean gum, cerebrosides, and blood group A and O substances.
L-Galactose	—	Combined in agar.
D-Allulose or D-psicose	—	Free in cane molasses.
D-Fructose	Levulose	Free in fruit juices, honey, and seminal fluid. Combined in energy carrier, sucrose; energy storage, inulins of dahlia, Jerusalem artichokes, grasses, and ti plant (see also p. 256).
L-Sorbose	—	In fermented juice of mountain ash berries ( <i>Sorbus accuparia</i> L.).
D-Fucose	6-Deoxy-D-galactose	Combined in Tamicojalap ( <i>Impomoea orizabensis</i> ).
L-Fucose	6-Deoxy-L-galactose	Combined in bladderwack, seaweed ( <i>Fucus</i> or <i>Ascophyllum nodosum</i> ), blood group A and O substances, and gum tragacanth.
L-Rhamnose	6-Deoxy-L-mannose	Combined as glycoside in lemon flavin from bark of oak species ( <i>Quercus tinctoria</i> Mich.).
D-Epirhamnose	6-Deoxy-D-glucose	Combined in karaya gum and as glycoside in quinovin of <i>Chinchona</i> bark.
Mycarose	—	Combined in antibiotic carbomycin (see p. 103).
Streptose	6-Deoxy-2-C-formyl-L-lyxose	Combined in antibiotic streptomycin (see p. 66).

(Continued)

TABLE I. Occurrence of Sugars (*Continued*).

Name	Products of hydrolysis <sup>a</sup>	Source
<u>Monosaccharides</u> ( <i>continued</i> )		
Digitoxose	2,6-Dideoxy-D-allose	Combined in digitalis glycosides (see Vol. 3, p. 213).
D-Glucosamine	2-Amino-2-deoxy-D-glucose	Combined in lobster shells as chitin; in cell walls as hyaluronic acid; as heparin, a blood-clotting factor; and as mucitinsulfuric acid, a mucus component.
D-Galactosamine	2-Amino-2-deoxy-D-galactose	Combined in a connective tissue substance, chondroitinsulfuric acid.
D-manno-Heptulose	--	Free in avocado or alligator pear ( <i>Persea gratissima</i> ).
Sedoheptulose	D- <i>altro</i> -Heptulose	Free in plants of <i>Sedum</i> species ( <i>Sedum spectabile</i> Bor.).
<u>Disaccharides</u>		
Sucrose <sup>b</sup>	D-Glucose, D-fructose	Free in juice of all land plants, in particular sugar cane ( <i>Saccharum officinarum</i> L.), sugar beet ( <i>Beta vulgaris</i> ), and sugar maple ( <i>Acer saccharum</i> ).
$\alpha,\alpha$ -Trehalose <sup>b</sup>	D-Glucose (2 molecules)	Free in rye ergot, yeast, young mushrooms, resurrection plant ( <i>Selaginella lepidophylla</i> ), and seaweeds.
Turanose	D-Glucose, D-fructose	Combined in the sugar melezitose.
Lactose	D-Glucose, D-galactose	Free in milk of all mammals and in one form of pollen from <i>Forsythia</i> .
Melibiose	D-Glucose, D-galactose	Combined in the trisaccharide raffinose.
Cellobiose	D-Glucose (2 molecules)	A component of hydrolyzate of cellulose.
Maltose	D-Glucose (2 molecules)	A component of hydrolyzate of starch or glycogen.
Isomaltose	D-Glucose (2 molecules)	A component of hydrolyzate of starch or glycogen arising from branching points of polysaccharide molecule.
Gentiobiose	D-Glucose (2 molecules)	Combined in glycoside amygdalin from almonds or in trisaccharide gentianose (see Vol. 2, p. 878).
<u>Trisaccharides</u>		
Maltotriose	D-Glucose (3 molecules)	A component in hydrolyzate of starch.
Panose	D-Glucose (3 molecules)	A component in hydrolyzate from starch or glycogen arising from branching points of molecule.
Gentianose <sup>b</sup>	D-Glucose (2 molecules), D-fructose (1 molecule)	Free in rhizomes of many species of <i>Gentiana</i> .

(Continued)

TABLE I. Occurrence of Sugars (Concluded).

Name	Products of Hydrolysis <sup>a</sup>	Source
<u>Trisaccharides (continued)</u>		
Melezitose <sup>b</sup>	D-Glucose (2 molecules), D-fructose (1 molecule)	Free in "honey dew" of limes and poplars, exudate from insect-produced wounds of Douglas fir and larch, and melezitose honey from these trees.
Raffinose <sup>b</sup>	D-Galactose, D-glucose, D-fructose	Free in sugar beet juice and sugar beet molasses (see <i>Molasses</i> ).
<u>Tetrasaccharides</u>		
Stachyose <sup>b</sup>	D-Galactose (2 molecules), D-glucose, D-fructose (1 molecule each)	Free in roots of mint family ( <i>Stachys</i> ), in soybeans ( <i>Soja hispida</i> ), and ash manna ( <i>Fraxinus ornus</i> ).
<u>Pentasaccharides</u>		
Verbascose <sup>b</sup>	D-Galactose (3 molecules) D-glucose, D-fructose (1 molecule each)	Free in certain <i>Verbascum</i> species (mullein).

<sup>a</sup> Unless otherwise indicated, all names refer to one molecule of sugar.

<sup>b</sup> These sugars are nonreducing; all other sugars are reducing.

### Occurrence

Not all the sugars are known to exist in nature. Some, for example D-mannose, had been synthesized before they were isolated from a natural source. Most naturally occurring sugars have been found combined as glycosides or as polysaccharides. Of the few sugars which exist in the free state, sucrose (XIV), D-glucose, and D-fructose are characteristic of the plant world. Lactose (XV) and D-glucose are characteristic of the animal kingdom. Most of the remaining sugars have been synthesized and/or isolated from natural sources.

Table I demonstrates the variety of places where sugars occur. This list by no means includes all the sugars that have been discovered and, in most cases, it includes only a few of the known sources.

### Physical and Chemical Properties

#### PHYSICAL PROPERTIES

Melting points, optical rotations (see *Polarimetry*), and crystalline forms for some sugars are given in Table II. Refractive indexes of several sugars are listed in Table I, p. 19.

Chromatography of sugars, in recent years, has developed into a most useful research tool. Each sugar or degradation product has characteristic partition coefficients. A shrewd selection of saccharophilic and saccharophobic solvents will separate sugar material on a variety of supporting mediums. In early work, magnesium silicate and various hydrated silicas were employed. Cellulose in columns or papers has gained a great popularity in more recent years. Activated carbon is a choice for aqueous solvents. Such procedures are so much more efficient that much of the early work is being repeated. Significant additions to the knowledge of sugar reactions are being gleaned from mixtures inseparable by older techniques.

TABLE II. Physical Properties of Some Sugars.

Sugar	Crystalline form	M.p., °C.	$[\alpha]_D^{20a}$
<b>Monosaccharides</b>			
$\alpha$ -D-Ribose	—	95	- 23.1 $\rightarrow$ - 23.7 (c = 4)
$\beta$ -L-Arabinose	Rhombic needles	160	+190.6 $\rightarrow$ +104.5
$\alpha$ -D-Xylose	Monoclinic	145	+ 93.6 $\rightarrow$ + 18.8 (c = 4)
D-Xylulose	—	—	+ 33.1 (c = 2)
$\alpha$ -D-Glucose	Orthorhombic sphenoidal	146	+112.2 $\rightarrow$ + 52.7 (c = 4)
$\alpha$ -D-Glucose monohydrate	Monoclinic hemimorphic	83	+102.0 $\rightarrow$ + 47.9 (c = 4)
$\beta$ -D-Glucose	Orthorhombic prisms	148-150	+ 18.7 $\rightarrow$ + 52.7 (c = 4)
$\alpha$ -D-Mannose	—	133	+ 29.3 $\rightarrow$ + 14.2 (c = 4)
$\beta$ -D-Mannose	Rhombic prisms	132	- 17.0 $\rightarrow$ + 14.2 (c = 4)
$\alpha$ -D-Galactose	Hexagonal prisms	167	+150.7 $\rightarrow$ + 80.2 (c = 5)
$\beta$ -D-Galactose	—	—	+ 52.8 $\rightarrow$ + 80.2 (c = 4)
$\alpha$ -D-Fructose	Rhombic prisms	102-104	-132.2 $\rightarrow$ - 92.4 (c = 4)
$\beta$ -D-Sorbose	Rhombic	159-161	- 43.7 $\rightarrow$ - 43.4 (c = 12)
$\beta$ -D-Epirhamnose	Needles	139-140	+ 73.3 $\rightarrow$ + 29.7 (c = 8)
$\alpha$ -L-Fucose	Needles	145	-152.6 $\rightarrow$ - 75.9 (c = 4)
$\alpha$ -L-Rhamnose mono-hydrate	Monoclinic	93- 94	- 8.6 $\rightarrow$ + 8.2 (c = 4)
$\beta$ -L-Rhamnose	Needles	123-125	+ 38.4 $\rightarrow$ + 8.9
D-manno-Heptulose	Prisms	152	+ 29.0
D-Heptulose	—	—	+ 2 to 3 (c = 10)
<b>Disaccharides</b>			
$\beta$ -Cellobiose	—	225	+ 14.2 $\rightarrow$ + 34.6 (c = 8)
$\alpha$ -Gentiobiose	—	85- 86	+ 21.4 $\rightarrow$ + 8.7 (c = 5)
dimethanolate	—	—	—
$\beta$ -Gentiobiose	—	190-195	- 11.0 $\rightarrow$ + 9.6
$\alpha$ -Lactose monohydrate	Monoclinic	202	+ 85.0 $\rightarrow$ + 52.6 (c = 8)
$\beta$ -Lactose	Monoclinic sphenoids	252	+ 34.9 $\rightarrow$ + 55.4 (c = 4)
$\beta$ -Maltose monohydrate	Needles	102-103	+111.7 $\rightarrow$ +130.4 (c = 4)
$\beta$ -Melibiose dihydrate	Monoclinic	82- 85	+111.7 $\rightarrow$ +129.5 (c = 4)
Sucrose	Monoclinic	160-186 <sup>b</sup>	+ 66.53 (c = 26)
$\alpha, \alpha$ -Trehalose dihydrate	Rhombic prisms	97	+178.3
Turanose	Prisms	157	+ 27.3 $\rightarrow$ + 75.8 (c = 4)
Gentianose	White tablets	209-211	+ 31.5
<b>Tri- and Tetrasaccharides</b>			
Melezitose dihydrate	Needles	153-154	+ 88.2 (c = 4)
Raffinose pentahydrate	Needles	80	+105.2 (c = 4)
Stachyose tetrahydrate	Rhombic tablets	167-170	+148

<sup>a</sup> The solvent in all cases is water, and the concentration is expressed in grams per 100 milliliters of solution.

<sup>b</sup> Depending upon solvent from which crystallized: H<sub>2</sub>O, 186°; CH<sub>3</sub>OH, 170°.

### CHEMICAL PROPERTIES

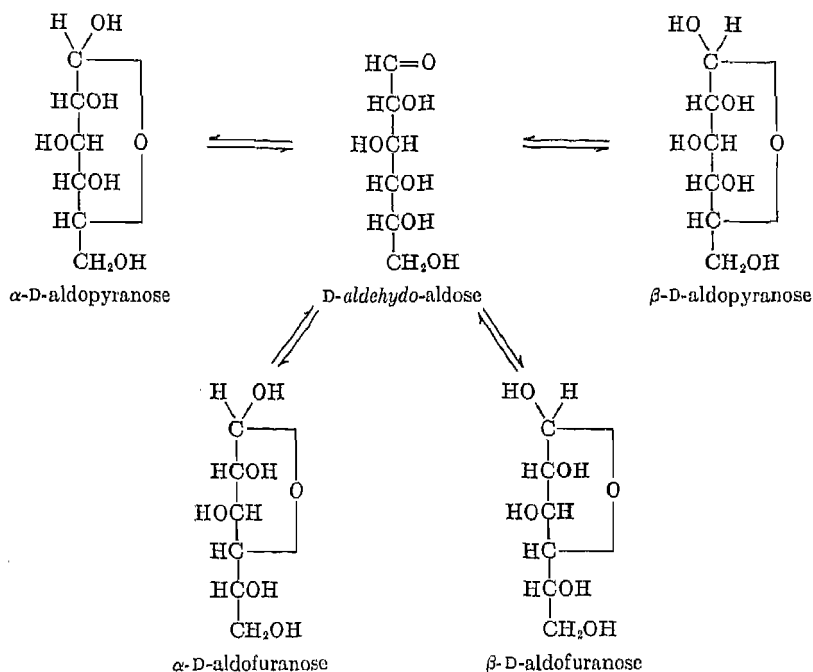
The carbonyl, primary and secondary hydroxyl, hemiacetal, and full acetal groupings present each contribute to the chemical properties of sugars. These properties will be discussed as general reactions, illustrated in some cases by specific examples. See also "Derivatives," p. 261; *Carbohydrates*.

**Mutarotation.** Determinations of optical rotation (see *Sugar analysis*) are complicated by changes in rotations of many sugars with the age of the solution. This phenomenon, called mutarotation, is caused by the establishing of an equilibrium

among the possible forms of a sugar. Two of these forms are cyclic hemiacetals formed by reaction of the carbonyl with a hydroxyl of the chain; the resulting 5- or 6-membered (furanose or pyranose) rings are stable in the solid state but labile in solution, particularly in the presence of acids or bases. The formation of the ring creates a new point of asymmetry at the carbonyl carbon. In the case of aldoses, two additional forms ( $\alpha$ - and  $\beta$ -) have been isolated, whereas no  $\alpha$ -form is known for ketoses.

The mutarotation of the aldoses therefore comes from equilibration of  $\alpha$ - and  $\beta$ - as well as furanose and pyranose forms. However, with ketoses, the mutarotation observed is ascribed to the furanose-pyranose equilibration. Some, but by no means all, of the possible components of an aldose equilibrium are shown in Scheme 4 for

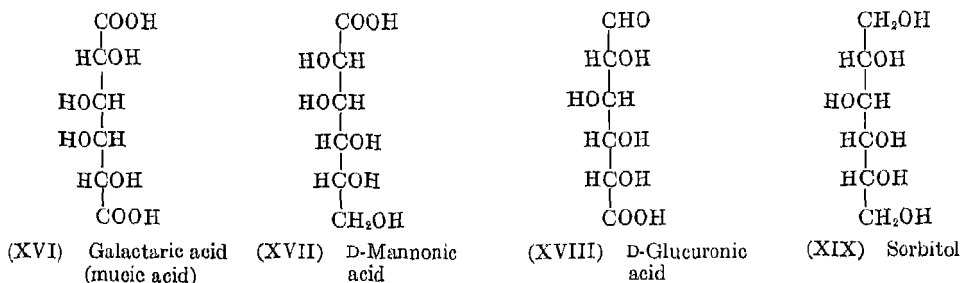
SCHEME 4



D-glucose. A D-sugar which upon mutarotation increases in positive optical rotatory power is in the  $\beta$ -anomeric form. An increase in the negative direction is evidence of the  $\alpha$ -anomer.

**Oxidation.** Strong oxidizing agents, such as chromic acid or alkaline permanganate, will convert sugars into carbonic and oxalic acids. Under milder conditions several intermediates may be obtained. In 30% nitric acid, both the carbonyl and primary hydroxyl groups react, yielding a *glycaric acid*, for example, galactaric acid (mucic acid) (XVI) from galactose. In alkaline hypobromite or hypoiodite only the carbonyl carbon of aldoses is attacked and a high yield of a *glyconic acid* or aldonic acid such as (XVII) is obtained. Although this reaction is not stoichiometric, it has been employed extensively in the determination of *reducing sugars* (in which a carbonyl or hemiacetal hydroxyl group is available—compare the formulas in Scheme 1 for lactose, a reducing sugar, and for sucrose, a nonreducing sugar). The traditional

methods of sugar determination depend upon the oxidation of the carbonyl by cupric ions in alkaline solution (Fehling's solution). (See also *Sugar analysis*.) If the carbonyl group is protected, for example by acetal formation, the terminal carbon atom may be oxidized to a carboxyl group, yielding a *glycuronic acid*, for example (XVIII).



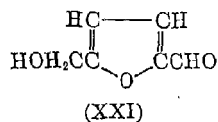
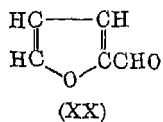
**Reduction.** Sugars can be reduced to polyhydric alcohols, some of which such as sorbitol (D-glucitol) (XIX) have considerable commercial importance (see *Alcohols, higher polyhydric*). The reaction was first achieved with sodium amalgam. An early commercial process utilized electroreduction at a cathode. Present methods employ pressure hydrogenations with activated nickel or platinum catalysts; on a laboratory scale metal hydrides are useful reagents.

With higher pressures and temperatures and a highly active nickel catalyst, hydrogenolysis takes place. The process was exploited by the Germans during World War II for the production of glycerol and glycols.

As a research tool in studying carbon chains, hydriodic acid has found some use in reducing a sugar to the corresponding alkyl iodide.

**Pyrolysis.** Heating sugars causes elimination of water and decomposition. Under some conditions, the product is more or less brown, with a characteristic taste and odor, and is called *caramel* (*q.v.*). This substance, obtained largely from dextrose (*q.v.*), finds extensive use in food and beverage industries, both for its color and its flavor. Components of the reaction mixture may run the gamut from simple monodehydrated derivatives to carbon. Because similar reactions occur in solution, it is necessary to exercise utmost caution in processing sugars and sugar derivatives.

When sugars are heated in the presence of strong acids, characteristic dehydrations occur giving significant yields of furfural derivatives. Pentoses and glycuronic acids yield furfural (*q.v.*) (XX). Hexoses yield 5-(*hydroxymethyl*)furfural (XXI),

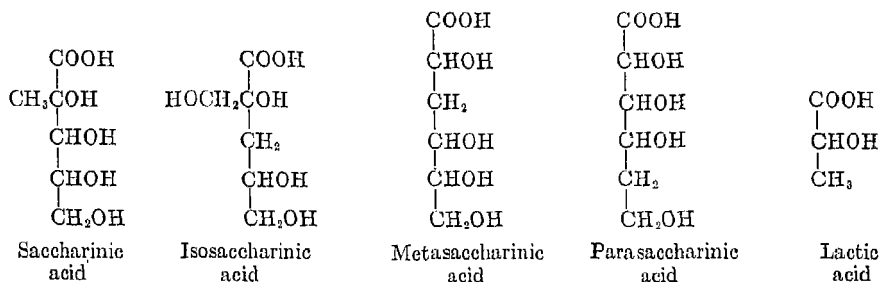


which upon further treatment may be converted to levulinic and formic acids (see p. 263). Furfural production from the xylans in oat hulls, corn cobs, and bagasse has become a large industry.

**Action of Alkalies.** In solution, dilute alkalies may cause enolization of the carbonyl group to form an enediol which may tautomerize to the original sugar, its *epimer* (with inverted configuration at the carbon atom adjacent to the carbonyl group), or the corresponding ketose (or aldose). This equilibrium reaction, discovered by Lobry de Bruyn and Alberda van Ekenstein, has been employed to clarify

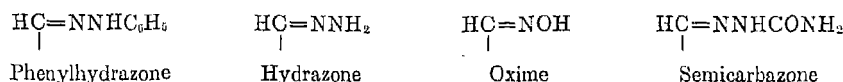
the relationships between sugars. The composition of the mixture varies with the base used. It has been reported that lead hydroxide produces D-mannose from D-glucose, but apparently no D-fructose, and sodium hydroxide produces D-fructose but very little D-mannose (6). See also Vol. 2, p. 873; Vol. 12, p. 852.

Nef found that stronger alkalis cause further enolization and result in degradation of the sugars. Saccharinic acids and lactic acid predominate in the reaction products. The reaction has been proposed as a method for the commercial production of lactic acid (*q.v.*).

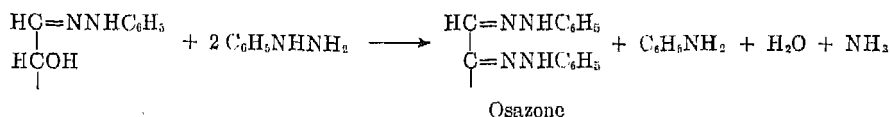


**Carbonyl Reactions.** The classic test reactions for carbonyl groups give somewhat anomalous results with sugars. For example, Tollens' reaction with ammoniacal silver nitrate indicates reducing action, but Schiff's test with sulfur dioxide-decolorized fuchsin fails.

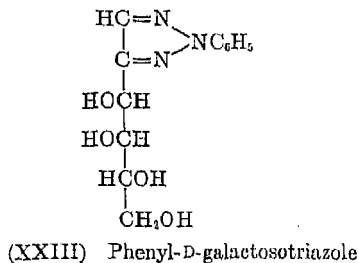
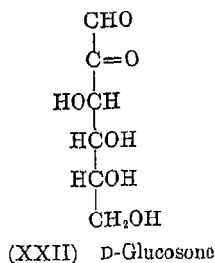
With phenylhydrazine, hydrazine, hydroxylamine, and semicarbazide, reactions are so characteristic that these substances have been called the sugar reagents. The products are substituted imines or imides:



If the phenylhydrazone is not insoluble (for example, mannose phenylhydrazone), further reaction involving two molecules of phenylhydrazine may occur to form an *osazone*:



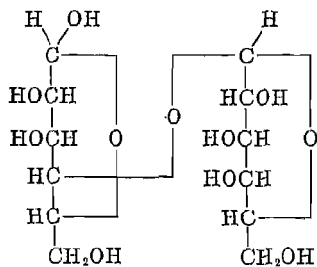
Osazones are frequently employed in the identification of sugars. *N*-Methyl-, 2,4-dinitro-, *p*-bromo-, and other substituted phenylhydrazines have been used to extend the usefulness of this reaction.



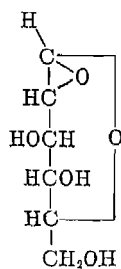
The imine moieties may be removed by hydrolysis in strong hydrochloric acid or transferred to benzaldehyde. Monosubstituted derivatives yield the original sugar; osazones yield 2-ketoaldoses called *osones* such as (XXII). Reduction of the osone with zinc and acetic acid yields the corresponding ketose. Cupric ions will oxidize an osazone to an *osotriazole* such as (XXIII).

**Glycoside Formation.** Glycosides (*q.v.*) are prepared by etherification reactions under restricted conditions. Arthur Michael reacted a glycosyl chloride with the potassium salt of a phenol. Fischer treated a sugar with alcoholic hydrogen chloride. Koenigs and Knorr reacted a glycosyl halide with an alcohol in the presence of silver carbonate. Michael's reaction is restricted to phenols, Fischer's to alcohols, but the Koenigs-Knorr is generally applicable for the production of  $\beta$ -glycosides. From the  $\beta$ -form the  $\alpha$ -form may be prepared by treatment with titanium tetrachloride or boron trifluoride. Acetylated  $\alpha$ -D-glycosyl bromide, one of the more common glycosyl derivatives, is frequently employed in glycoside syntheses.

Synthesis of oligo- and polysaccharides, which may be considered special examples of glycosides, has usually been achieved by modifications of the reactions discussed. Various synthetic tricks have been devised to overcome difficulties in obtaining a desired anomer. Lactose (XV) was obtained in Hudson's laboratory from tetra-*O*-acetyl- $\alpha$ -D-galactopyranosyl bromide and 1,6-anhydro- $\beta$ -D-mannopyranose, followed by epimerization of the resulting epilactose (XXIV) (7). Chemical synthesis of sucrose (XIV) was not achieved until 1953 when Lemieux and Huber found that triacetylated Brigl's anhydride (XXV) would combine with penta-*O*-acetyl-D-fructofuranose to produce the sucrose structure in very small yield (10).



(XXIV) Epilactose



(XXV) Brigl's anhydride

**Esterification.** Sugars are easily esterified by reaction with acids or their derivatives. Organic acid anhydrides of low-molecular-weight acids in pyridine at room temperature yield mainly the anomer analogous to the sugar form. At elevated temperatures, the sodium salt of the acid in the acid anhydride yields the  $\beta$ -D-anomer. Esters of acetic, propionic, butyric, benzoic, and *p*-toluenesulfonic acids are commonly prepared. See also "Derivatives"; *Carbohydrates*.

Sugar esters of organic acids are of some importance because they are more soluble in nonaqueous solvents than the free sugar. The stability such ester groups impart to the molecule, in many cases, has allowed isolation of sugars or other derivatives by methods, for example, distillation, which would have destroyed the substances themselves.

Boric esters are of interest from several angles. Some information can be gained about the structure of a polyhydroxy molecule by its effect on the ionization of boric acid. The same property has made possible chromatographic separations on ion-

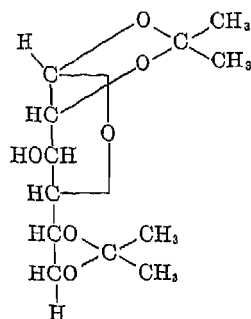


exchange materials. In other cases, stability of the boric ester has further complicated isolation of sugars.

**Etherification.** The classic methods of etherification apply to sugars (see Vol. 2, p. 875). More recent methods for special applications have included sodium catalysis of reaction with methyl iodide in liquid ammonia and methylation with diazomethane. Ethyl, benzyl, and other ethers are prepared by appropriate modifications of these reactions.

One ether which merits specific mention is the *triphenylmethyl* or *trityl ether*. Here the bulk of the aryl moiety is so great that only primary hydroxyl groups react. Hence, the extent of the reaction can elucidate structures of carbohydrates by determination of the number of end ( $-\text{CH}_2\text{OH}$ ) groups.

Special types of ethers, the *acetal* or *ketal* derivatives, have been of considerable interest, as in the Reichstein synthesis of ascorbic acid (see Vol. 2, p. 154). For example, acetone will react with glucose in the presence of a Lewis acid catalyst with the formation of an *isopropylidene* derivative (XXVI). In this case the derivative is of significance for several reasons. The hydroxyl on carbon number 3 is open and available for derivatization. Careful acid hydrolysis preferentially frees the 5,6-*O*-isopropylidene group; this provides a means of preparing the furanose derivatives of D-glucose. Benzaldehyde, formaldehyde, cyclohexanone, acetaldehyde, and other aldehydes and ketones have been employed in preparing these derivatives.



(XXVI) 1,2:5,6-Diisopropylidene- $\alpha$ -D-glucopyranose

**Replacement of Hydroxyl.** Removal of oxygen by replacement of hydroxyl with hydrogen at any but the anomeric carbon produces a *deoxy sugar*. 2-Deoxy-D-ribose is encountered in nucleic acids (*q.v.*). Rhamnose, L-fucose, and streptose have more or less widespread occurrence in biological materials.

Several methods for replacing a hydroxyl group have been developed to achieve substitution at a desired carbon. A toluenesulfonic ester group can be replaced with iodide which, in turn, is removed by catalytic hydrogenation. With ammonia the iodide or the toluenesulfonic ester may yield an amino sugar. Replacement of the toluenesulfonic ester is usually accompanied by a Walden inversion. Hence, only from a primary toluenesulfonic ester can there be expected to be obtained the derivative with the configuration of the original sugar.

**Complex Formation.** The polyhydroxy nature of sugars contributes to the formation of complexes with salts; thus lactose and sucrose complex with sodium chloride. In some cases, the complex can contribute to resolving a mixture, as in the isolation of xylose by its crystalline addition compound with calcium bromide. Salt complexes

have economic significance for they limit the extent to which molasses or hydrol (mother liquor from dextrose manufacture; see Vol. 4, p. 965) can be exhausted. On the other hand, the Steffen process (see *Molasses; Sugar manufacture*) exhausts beet molasses by forming the complex of sucrose with calcium hydroxide (commonly called "calcium saccharate," although it is not a salt of saccharic acid).

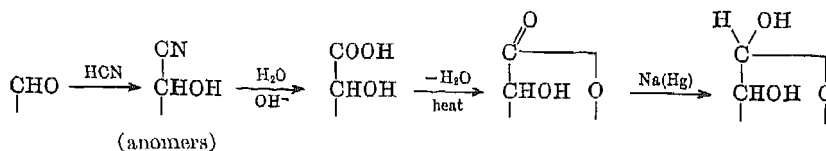
### Synthesis

Historically, the methods of sugar synthesis are of considerable importance. By lengthening and shortening the sugar chains, relationships of sugar structures were established. Indeed, many of the fundamentals of stereochemistry stem from this work. Furthermore, many sugars not available from natural sources can be synthesized. For example, while D-glucose is well-known, L-glucose is very rare, but might be made by combinations of these methods.

Of the various methods discussed, the Kiliani and Sowden-Fischer methods of increasing chain length and the Wohl, Zemplen, and Fischer methods of degradation are probably the most widely useful. Other tricks of synthesis are known. For example, D-mannitol readily forms a 1,2-5,6-diisopropylidene derivative. Periodate oxidation of this derivative followed by hydrolytic removal of the acetone yields optically pure D-glyceraldehyde.

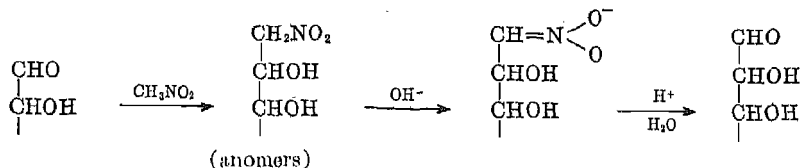
#### LENGTHENING CHAINS

**Kiliani Synthesis.** Hydrogen cyanide adds to a carbonyl group to give a cyanohydrin. One isomer of the newly created stereoisomeric pair usually predominates (*asymmetric synthesis*). Hydrolysis in alkaline solution followed by dehydration of the glyconic acid yields a lactone, which is reduced to a sugar with sodium amalgam or with an alkali metal hydride:

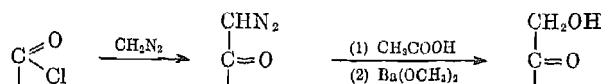


With aldoses, the next homolog is produced in about 25-50% over-all yield; ketoses give branched-chain sugars. Thus glucose yields the cyanohydrin, glucoheptonic acids and their lactones, and finally glucoheptoses.

**Sowden-Fischer Nitroparaffin Synthesis.** Nitroparaffins add to the carbonyl group. In alkaline solution a salt of a nitronic acid is formed. Acid hydrolysis of this salt gives up to a 50% over-all yield of a sugar of increased chain length:



**Diazomethane Synthesis.** A glyconoyl chloride will react with diazomethane to produce a ketose:

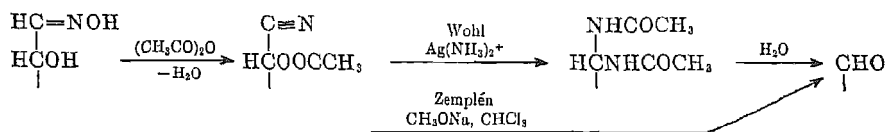


**Glyoxylic Ester Synthesis** (ref. 12, p. 121). A benzoin-type condensation occurs between ethyl glyoxylate and a sugar in the presence of a cyanide. Reduction of the carbonyl to hydroxyl and of the ester to aldehyde can produce several types of sugars.

**Grignard Synthesis of Sugars.** Grignard reagents adding to a glyconic ester will, under some conditions, produce modified types of ketoses.

#### DEGRADING CHAINS

**Wohl Degradation.** A sugar oxime is both acetylated and dehydrated to a nitrile with acetic anhydride. The nitrile is degraded with the diamminesilver ion to a diacetamide of the sugar with one less carbon. Hydrolysis of the diacetamide releases the sugar. Zemplén found that sodium methoxide in chloroform was superior for hexoses and higher sugars:

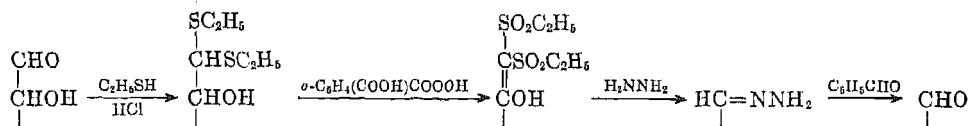


The use of strong ammonia (28%) has been suggested as being a further improvement in the technique.

**Ruff Degradation.** A calcium glyconate is degraded with hydrogen peroxide in the presence of ferric ion to yield a mixture of the next lower glyconic acid and the corresponding sugar. Yields of the reaction are of the order of 30%. See p. 266.

**Weerman Reaction.** A glyconic acid amide is degraded with hypophalite by the Hofmann rearrangement to yield the sugar with one less carbon atom.

**H. O. L. Fischer Degradation.** A diethyl mercaptal derivative of a sugar is oxidized with peroxyphthalic acid to a disulfone; hydrazine degrades this sulfone



to a hydrazone from which the lower homolog can be liberated with benzaldehyde.

#### Bibliography

- (1) A.C.S. Committee on Nomenclature, Spelling, and Pronunciation, *Chem. Eng. News*, **26**, 1622-28 (1948); **31**, 1776-82 (1953).
- (2) Bates, F. J., et al., "Polarimetry, Saccharimetry and the Sugars." *Natl. Bur. Standards (U.S.), Circ.*, **C440** (1942).
- (3) Browne, C. A., and Zerban, F. W., *Sugar Analysis*, Wiley, N.Y., 1941.
- (4) Deerr, N., *The History of Sugar*, Chapman & Hall, London, 1949.
- (5) Elsner, H., *Kurzes Handbuch der Kohlenhydrate*, Barth, Leipzig, 1935.
- (6) Gottfried, J. B., and Benjamin, D. G., *Ind. Eng. Chem.*, **44**, 141 (1952).
- (7) Haskins, W. T., Hann, R. M., and Hudson, C. S., *J. Am. Chem. Soc.*, **64**, 1852-56 (1942).
- (8) Honig, P., *Principles of Sugar Technology*, Elsevier, N.Y., 1953.
- (8a) Hudson, C. S., et al. (eds.), *Advances in Carbohydrate Chemistry*, Academic Press, N.Y., Vols. I-IX, 1945-54.

- (9) Lederer, R., and Lederer, M., *Modern Chromatography*, Elsevier, N.Y., 1953.
- (10) Lemieux, R. U., and Huber, G., *J. Am. Chem. Soc.*, **75**, 4118 (1953).
- (11) Percival, E. G. V., *Structural Carbohydrate Chemistry*, Prentice-Hall, N.Y., 1950.
- (12) Pigman, W. W., and Goepf, R. M., Jr., *Chemistry of the Carbohydrates*, Academic Press, N.Y., 1948.
- (13) Spencer, G. L., and Meade, G. P., *Cane Sugar Handbook*, 8th ed., Wiley, N.Y., 1944.
- (14) Vogel, H., and Georg, A., *Tabellen der Zucker und ihrer Derivate*, Springer, Berlin, 1931.
- (15) Whistler, R. L., and Smart, C. L., *Polysaccharide Chemistry*, Academic Press, N.Y., 1953.

J. L. HICKSON

## COMMERCIAL SUGARS

The few sugars which have achieved commercial significance have done so largely as foods for man, animals, or fermenting organisms since chemists, in general, have neglected to consider sugars as starting materials for chemical processing.

### Lactose

Lactose, U.S.P. XIV (4-*O*- $\beta$ -D-galactopyranosyl-D-glucopyranose, lactobiose) (XV), p. 231,  $C_{12}H_{22}O_{11}$ , formula weight 342.30, was unknown until 1628 when Fabritius Bartoletus of Mantau reported an "essential salt" in milk serum. Glucose was identified as one of its components in 1812, and galactose in 1855, but the structure of lactose evaded definition until 1927. The ordinary lactose of commerce is  $\alpha$ -lactose monohydrate. The sugar was synthesized by Haskins, Ham, and Hudson (1). See also *Dairy products (by-products)*.

Lactose occurs in the milk of all species of mammals, including the whale, ranging in amount from 1.8% in rabbit milk to over 7% in ass and elephant milk. Cow's milk contains 2.9-5.3% lactose and human milk 4.0-8.3%. Production of lactose was begun before 1880 in the Swiss canton of Luzern. One New York firm in 1893 reported a production of 250,000 lb. In 1952, from a potential of about 270 thousand short tons in commercial milk, about 20 thousand short tons entered the United States' market as the sugar lactose.

### PHYSICAL AND CHEMICAL PROPERTIES

Lactose is a water-soluble substance prepared in three crystallized forms:  $\alpha$ -Lactose monohydrate crystallizes from aqueous solution below 93.5°C. as rhombic sphenoidal crystals, stable in air; m.p. 201.6°C.,  $d_4^{20}$  1.525.  $\beta$ -Lactose anhydrate is prepared by crystallization from solution above 93.5°C. as transparent, colorless crystals of the holaxial-polar class of the monoclinic system, stable under reasonable humidity conditions; m.p. 252.2°C.  $\alpha$ -Lactose anhydrate is metastable to atmospheric moisture; m.p. 222.8°C.,  $d_4^{20}$  1.589. All forms are soluble in water, liquid ammonia, and acetic and formic acids; they are slightly soluble in 85% methanol and pyridine; and insoluble in ethyl alcohol, absolute methanol, ether, and chloroform. Water solubility is the outstanding physical property (see Vol. 4, p. 842). A definite break in the solubility curve at a temperature of 93.5° has been found to occur at the transition point, in solution, for  $\alpha$ - and  $\beta$ -lactose.

Somewhat astonishingly, for a sugar, lactose is not very sweet (see Table I, p. 248); therefore, milk-based desserts usually call for additional sweetening.

Unlike sucrose, lactose is a reducing sugar.

**Hydrolysis.** Lactose hydrolysis is catalyzed by acids or by enzymes (lactases)

from many sources. The reaction is monomolecular. Practical preparations of hydrolyzed lactose sirup are made by heating 10–30% solutions adjusted to pH 1.2–1.3 with hydrochloric or sulfuric acid, as well as through the action of lactases.

Lactases widely distributed throughout microorganisms, plants, and animals, are of two kinds,  $\beta$ -D-galactosidases and  $\beta$ -D-glucosidases. Typical of the  $\beta$ -D-galactosidases are those of the *Torula* yeasts. Emulsin from bitter almonds contains a typical  $\beta$ -D-glucosidase lactase.

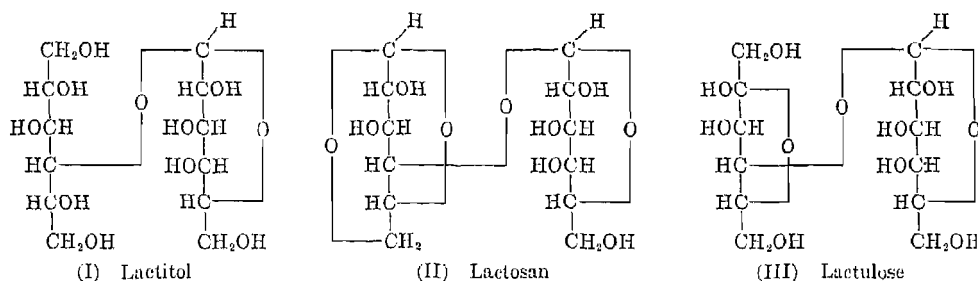
**Fermentation.** The best-known fermentation of lactose occurs in the souring of milk to form lactic acid. A number of organisms cause this reaction; examples are *Streptococcus lactis* and *Lactobacillus casei* (see Vol. 4, p. 843; Vol. 8, p. 172). Propionic acid in 48% yield can be made by a mixed culture of *Propionibacterium shermanii* and *L. casei*. Ethyl alcohol can be produced in 80–83% yield by *Torula lactosa*.

**Oxidation.** Nitric acid in various concentrations degrades lactose to galactaric and D-glucaric acids or to tartaric, oxalic, and carbonic acids. Milder acid agents produce D-gluconic and D-galactonic acids. Iodine, bromine, or copper in alkaline solutions will give lactobionic acid. Periodic acid yields tartronic, glycolic, glyceric, and formic acids and formaldehyde.

**Reduction.** Sodium amalgam was reported, in 1872, to degrade lactose to galactitol, glycerol, ethyl alcohol, isopropyl alcohol, isohexyl alcohol, and sodium lactate. Catalytic hydrogenation has produced *lactitol* (I). Under more drastic conditions, such as a copper–chromium oxide catalyst, 300 atm., and 250°C., a variety of reductive degradation products is obtained, including 4-hydroxytetrahydrofurfuryl alcohol, and several hexamethylenetriols.

**Degradation.** Darkening is encountered to some extent in the pasteurization, evaporation, and drying of milk. *Lactosan* (II) has been identified among the intermediate degradation products. Caramel from lactose is a substitute for that from dextrose.

**Action of Alkali.** This follows the expected pathways (see p. 238) varying from epimerization to the formation of saccharinic acids. One new product is *lactulose* (III).



**Carbonyl Reactions.** Lactose phenylosazone was among the first reported by Emil Fischer in 1884. Considerable study has been made of the structure and the properties of this osazone for it was obtained from one of the few saccharides higher than monosaccharides that could be prepared in a high state of purity.

**Lactoside Formation.** Physiologically active substances such as the sterols or sulfa compounds have been solubilized by conversion to the lactosides. They have, however, received no widespread use in medicine.

**Esterification.** Acetates, propionates, benzoates, isocyanates, *p*-nitrobenzoates,

nitrate, and phosphates have been described. The octanitrate has received some attention as an explosive (see p. 264).

#### MANUFACTURE

Industrial sources of lactose include skim milk, whey, and buttermilk (see Vol. 4, p. 840). Lactose is produced in four grades. A crude product may contain 2% protein and may develop an odor on standing. Crude lactose is converted to a technical grade by defecation of protein and decolorizing with carbon. The technical grade is suitable for infant foods, fermentation, and explosives. Careful purification to meet rigid specifications for heavy metals and purity will produce U.S.P. lactose. A bacteriological grade for culture media meets requirements of freedom from growth factors and contaminating organisms.

#### PHYSIOLOGICAL PROPERTIES

Lactose has been highly recommended in infant formulations, although it may be that interpretation of the evidence has been colored, too frequently, by partisan attitudes. Otherwise, lactose is physiologically significant in two respects.

At high levels in the diet (40–80%) rats develop marked changes in the cornea that almost invariably progress to bilateral cataract. In some cases, there is an accompanying excessive calcium content that can be ascribed to the whole lactose molecule. The cataracts are due, however, solely to the galactose moiety. Riboflavin, to some extent, delays the onset of the cataracts but the complete etiology is not known.

At lower levels, the unabsorbed part of dietary lactose contributes to a change in the nature of the intestinal flora. The change from primarily putrefactive to acidogenic organisms is believed to be favorable in the treatment of some digestive disorders.

### Maltose

Maltose (4-*O*- $\alpha$ -D-glucopyranosyl-D-glucopyranose, maltobiose),  $C_{12}H_{22}O_{11}$ , formula weight 342.30, is a disaccharide composed of two D-glucose residues.

The free sugar rarely occurs in nature. More frequently it is encountered as a component of partially hydrolyzed starch. First preparation has been ascribed to de Saussure in 1819, although the identity of his product was not recognized until 1847 (6).

#### PHYSICAL AND CHEMICAL PROPERTIES

Maltose, m.p. 102–103°C.,  $[\alpha]_D^{20} +111.7^\circ \rightarrow 130.4^\circ$  ( $H_2O$ ,  $c = 4$ ),  $d_{20}^{20}$  1.540, is soluble in water, slightly soluble in ethyl alcohol, and insoluble in ether. It crystallizes from water or dilute ethyl alcohol as a stable monohydrate of the  $\beta$ -anomer. It is about a third as sweet as sucrose.

Maltose is a reducing sugar. Emil Fischer, in 1889, oxidized maltose to maltobionic acid and showed that it was a glucosylglucose. Attachment at the fourth carbon was demonstrated by the methylation work of Haworth and Peat in 1926.

Many of the traditional ester, ether, and carbonyl derivatives of maltose have been prepared. Their properties can be found in the compendia of Bates; Elsner; or Vogel and Georg (3,5,7). No derivative has attained any commercial significance.

The principal useful properties of maltose are its ready fermentability by most yeasts and its ready digestibility.

#### MANUFACTURE

There have been several reports of the occurrence of free maltose in the plant world. It has been alleged to comprise 50% of the carbohydrate of *Tropaeolum* leaves and up to 1.25% of those of *Pyrola rotundifolia*, *Populus tremuloides*, and *Linnaea borealis*. Commercially, however, it is produced exclusively by hydrolysis of starch from grains (wheat, barley, or corn) or tubers (potato or manioc). It is a major component of corn sirups (see *Dextrose and starch sirups*) and malt (see *Beer and brewing*). Maltose is usually isolated by enzymic (diastase or a  $\beta$ -amylase) hydrolysis from impure forms of the sugar, malt, malt sirup, or maltose sirup.

*Malt sirup* is essentially a solution of maltose with a characteristic flavor. Refining this sirup removes the malt flavor and the product is *maltose sirup*.  $\beta$ -Amylase enzymes of *Aspergillus niger* or *Aspergillus oryzae* convert wheat flour to maltose to the extent of 75–85%. Removal of protein and carbon treatment give a 75% solution called maltose sirup. Malt sirup was produced to the extent of 200 million pounds in 1945 (4), but the demand for it has since decreased.

**Uses.** Untold amounts of maltose are produced by the malting process for captive consumption in the brewing industry. In addition to its presence in beer, malt, and corn sirup, maltose is added to soft drinks, bread doughs, confections, infant and invalid foods, yeast, bee food, printing compositions, snuff, and stamp-pad compositions. Malt sirup finds use as a flavor component in ice cream, particularly in chocolate flavors, and in baking.

#### Sucrose

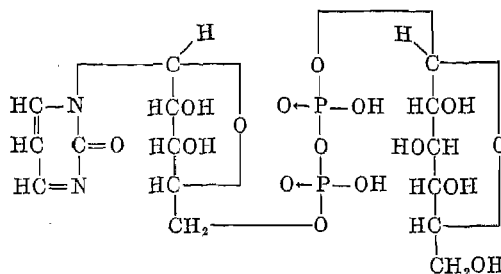
Sucrose, N.F. IX ( $\alpha$ -D-glucopyranosyl  $\beta$ -D-fructofuranoside) (XIV), p. 231,  $C_{12}H_{22}O_{11}$ , formula weight 342.30, is a disaccharide composed of D-glucose and D-fructose. Its use was at first restricted to the wealthy owing to its early high price, but ancient Chinese doctors and those of other early people prescribed it as a medicinal. Today our sirups, elixirs, and pills still are compounded with sugar. Queen Elizabeth I is credited with introducing sugar to the table, a custom which has spread throughout the world.

Sucrose is said to be the first pure carbohydrate to separate from the photosynthetic process. As such, it is the progenitor of all plant and animal substances and the origin of coal and petroleum, our principal sources of heat and power. Sucrose is found in almost all land plants, in the juice, seeds, flowers, leaves, stems, and roots.

Commercially, sucrose is produced in the tropics and semitropics from the juice of the sugar cane (*Saccharum officinarum* L.). In temperate zones sources are the sugar beet (*Beta vulgaris*), sorghum (*Sorghum vulgare*), and the sugar maple (*Acer saccharum*). Beets provide much of the sugar for Europe and central and western United States. Cane supplies the sugar requirements of almost all of the rest of the world. Sorghum, repeatedly suggested as a source, continues to be used to a limited extent, mostly to produce a sirup. Maple sugar has a limited production which is practical only because the product commands a premium price. Neither sorghum nor maple sugar is a serious competitor for the sugar market. See also *Sugar manufacture*.

Synthesis of sucrose defied efforts until 1943, when Hassid, Doudoroff, and Barker

found that a phosphorylase enzyme from *Pseudomonas saccharophila* D. would combine glucose 1-phosphate with fructose to make sucrose (9). The active intermediate recently has been identified as *uridinediphosphoglucose* (uridine 5'-pyrophosphate glucose ester) (IV) (12). The chemical synthesis (see p. 240) was achieved only in 1953 (13).



(IV) Uridinediphosphoglucose

## PHYSICAL AND CHEMICAL PROPERTIES

Sucrose, is a water-soluble substance which crystallizes in a characteristic monoclinic form: m.p. about 184°C. (solvent of crystallization, water) with some decomposition;  $d_{17.6}^{17.6}$ , 1.58046; it is readily soluble in dilute water, ethyl alcohol, and ammonia, practically insoluble in anhydrous ethyl alcohol, ether, chloroform, and anhydrous glycerol.

The most outstanding physical property of sucrose is its sweet taste. In comparing sweetness, sucrose is frequently used as the standard substance with a value of 100 (see Table I (14)). The relative sweetness of fructose is dependent upon temperature and concentration. At 5°C., fructose is 1.437 times as sweet as sucrose; at 40°C., they have equal sweetness; while at 60°C., fructose is only 0.79 times as sweet as sucrose.

The second most obvious property of sucrose is its solubility in water (8,11).

TABLE I. Relative Sweetness of Sugars in 10% Solutions.

Fructose.....	120	Galactose.....	67
Sucrose.....	100	Mannitol.....	64
Glycerol.....	77	Lactose.....	39
Glucose.....	69		

Extensive tables of the optical properties of sucrose have been compiled because of the importance of the refractive index and optical rotation in sugar manufacture (3,11,16). See also *Sugar analysis*.

Sucrose has two predominating chemical properties: it is nonreducing and readily hydrolyzed.

Sucrose is called nonreducing since it fails to reduce copper in Fehling's or equivalent tests inasmuch as the reducing groups of both moieties are tied up as glycosides. More vigorous reagents, however, readily attack the sucrose molecule and account for some use of sucrose as an antioxidant, for example, in jams and jellies. Fermentation and other degradations of sucrose are the most important industrial (nonfood) applications. See also "Derivatives."



**Hydrolysis.** Although the glycosidic linkage is relatively stable in dilute alkali and in neutral solutions, maximum stability occurs at about pH 9. Sucrose is easily hydrolyzed by acids and certain enzymes to a mixture of D-glucose and D-fructose, called "invert sugar" because of a reversal of the direction of optical rotation. Several acids exhibit remarkable variance in their ability to cause inversion (see Table II).

TABLE II. Inverting Power of Acids.

Acid	Inverting power	Acid	Inverting power
Hydrobromic.....	111.4	Phosphoric.....	6.21
Hydrochloric.....	100.0	Citric.....	1.72
Nitric.....	100.0	Formic.....	1.53
Methanesulfonic.....	100.0	Malic.....	1.27
Sulfuric.....	53.6	Lactic.....	1.07
Oxalic.....	18.57	Acetic.....	0.40

Source: reference (16).

Production of invert sugar by acid hydrolysis under extreme conditions may result in a loss of 7-8% of the fructose. The lost fructose to some extent can be identified as fructose dianhydrides. Enzymic (invertase) inversion can compete with the acid process because similar losses are not sustained. Invertase inversion also finds favor by those who are prejudiced against chemical alteration of a food substance.

Although invert sugar sirup is an item of commerce, many consumers prepare their own by adding 1 part of citric or tartaric acid to 800 parts of sucrose in 33-35% solution and heating at 80°C. for half an hour.

**Fermentation.** Sucrose, as a component of molasses (*q.v.*), was for many years a chief source of industrial and potable alcohol from yeast fermentation. Other substances produced in commercial quantities are listed in Table III (see also *Alcohol, industrial; Fermentation*; and articles on the specific compounds). Dextran is used as a plasma expander (*q.v.*).

TABLE III. Fermentation Products from Sucrose.

Products	Organisms	Percentage yield
Acetone } 1-Butanol }	<i>Clostridium acetobutylicum</i>	9 18
Citric acid	<i>Citromyces</i> or <i>Aspergillus niger</i>	50
Dextran	<i>Leuconostoc mesenteroides</i> or <i>L. dextranicum</i>	25
Fumaric acid	<i>A. fumaricus</i> or <i>Rhizopus nigricans</i>	50
D-Gluconic acid	<i>Penicillium chrysogenum</i> or <i>A. niger</i>	50
Itaconic acid	<i>A. terreus</i>	15
Kojic acid	<i>A. flavus</i> or <i>A. oryzae</i>	60
Lactic acid	<i>R. oryzae</i>	95

**Oxidation.** Vigorous oxidation of sucrose with strong nitric acid produces equimolar quantities of oxalic acid (*q.v.*) and tartaric acid (*q.v.*).

**Hydrogenation.** In the presence of a Raney-nickel catalyst, inverted sucrose is hydrogenated to a mixture of sorbitol and D-mannitol. See also *Alcohols, higher polyhydric*, Vol. 1, pp. 324, 328.

**Hydrogenolysis.** Under more drastic conditions the sugar chains are severed and good yields of glycerol (*q.v.*) and propylene glycol (see Vol. 7, pp. 240, 252) are

formed. The reaction is frequently performed in two stages, the first producing the sugar alcohol and the second accomplishing the cleavage. Cleavage occurs at 225–235°C. and 80–100 atm. in the presence of a nickel catalyst. The addition of less than 1% of an alkali metal salt is said to raise the glycerol yield to more than 80% (20). A major plant installation is being built to apply this process.

**Alkaline Degradation.** Sucrose autoclaved with aqueous calcium hydroxide yields up to 70% of lactic acid (*q.v.*).

**Acid Degradation.** Hot mineral acids convert sucrose to 5-(hydroxymethyl)-furfural. By variations, the reaction can yield equimolar amounts of levulinic and formic acids (*q.v.*) (see p. 263).

#### MAPLE SUGAR AND MAPLE SIRUP

Maple sugar and maple sirup are forms of sugar with a characteristic flavor and aroma. They are prepared by concentrating a sap collected from several varieties of maple, principally the sugar maple (*Acer saccharum*) and the black maple (*Acer saccharum nigrum*) which grow throughout the northeastern United States and southeastern Canada.

Average results of analyses of fifty samples of maple sap are: total solids, 3.25%; sucrose, 2.93; invert sugar, 0.021; ash, 0.0396. The characteristic flavor is developed during the concentration. Sap which has been freeze-dried has none of it. By modifying the technique of evaporation, it was found practical to obtain a fourfold intensification of the maple flavor (20). Identity of the flavor component is as yet unknown. There is on the market a "maple-flavor" which is alleged to be 3-methyl-1,2-cyclopentadione. This is of interest because of its structural similarity to a tautomer of reductic acid (3-hydroxy-1,2-cyclopentadione), a product of sugar degradation (15).

Maple sirup is prepared by evaporating maple sap at atmospheric pressure until its boiling point rises to 219°F. or until the specific gravity rises to 35.6° Bé. at 60°F. Under these conditions, the sirup will contain not less than 65% total solids and weigh not less than 11 lb. per U.S. gallon. To produce maple sugar, sirup is concentrated until the boiling point rises to 240–250°F. and allowed to crystallize. Yields run about 40 gal. of sirup or 300 lb. of sugar from 100 trees per season (18).

Consumption in the U.S. during 1951 totaled 23,851,000 lb. of maple sugar, including the sugar equivalent of 2,086,000 gal. of maple sirup. Of this total, 9,547,000 lb. was imported from Canada (17).

#### Bibliography for Lactose, Maltose, and Sucrose

##### LACTOSE

- (1) Haskins, W. T., Hann, R. M., and Hudson, C. S., *J. Am. Chem. Soc.*, **64**, 1852–56 (1942).
- (2) Whittier, E. O., and Webb, B. H., *By-products from Milk*, Reinhold, N.Y., 1950.

##### MALTOSE

- (3) Bates, F. J., *et al.*, "Polarimetry, Saccharimetry and the Sugars," *Natl. Bur. Standards (U.S.), Circ.*, **C440** (1942).
- (4) Effron, A., and Bloom, R. H., *Ind. Eng. Chem.*, **40**, 412–15 (1948).
- (5) Elsner, H., *Kurtzes Handbuch der Kohlenhydrate*, Barth, Leipzig, 1935.
- (6) Harding, T. S., *Sugar*, **25**, 350–52 (1923).
- (7) Vogel, H., and Georg, A., *Tabellen der Zucker und ihrer Derivate*, Springer, Berlin, 1931.

## SUCROSE

- (8) Benrath, A., *Z. anorg. allgem. Chem.*, **249**, 245 (1942).
- (9) Hassid, W. Z., Doudoroff, M., and Barker, H. A., *J. Am. Chem. Soc.*, **66**, 1416 (1944).
- (10) Herzfeld, A., *Z. Ver. Rübenzuckerind.*, **42**, 181 (1892).
- (11) Honig, P., *Principles of Sugar Technology*, Elsevier, N.Y., 1953.
- (12) Leloir, L. F., and Calib, E., *J. Am. Chem. Soc.*, **75**, 5445 (1953).
- (13) Lemieux, R. U., and Huber, G., *J. Am. Chem. Soc.*, **75**, 4118 (1953).
- (14) Moncrieff, R. W., *Flavours*, **11**, No. 6, 5-11 (1948).
- (15) Sattler, L., private communication.
- (16) Spencer, G. L., and Meade, G. P., *Cane Sugar Handbook*, 8th ed., Wiley, N.Y., 1944, p. 354.  
Table II courtesy John Wiley & Sons, Inc.
- (17) U.S. Dept. Agr., *Agricultural Statistics*, Tables 138, 140, and 636 (1953).
- (18) U.S. Dept. Agr., *Farmers Bull.*, **1336** (1937).
- (19) Wiggins, L. F., *The Utilization of Sucrose*, Sugar Research Foundation, N.Y., 1950.
- (20) U.S. Pat. 2,335,731 (Nov. 30, 1943), R. R. Bottoms.
- (21) U.S. Pat. 2,549,877 (April 24, 1951), C. O. Willits and W. L. Porter (to U.S.A.).

J. L. HICKSON

## Invert Sugar

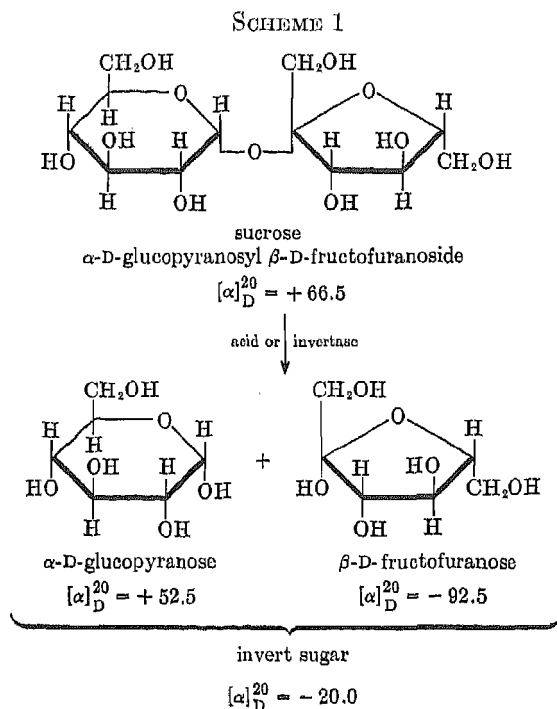
Invert sugar, so-called because the optical rotation of a sucrose solution is changed or inverted from dextrorotatory to levorotatory upon hydrolysis, is an equimolecular mixture of D-glucose (dextrose (*q.v.*)) and D-fructose (levulose) (see p. 256). Therefore, its properties are a composite of the properties of these two sugars. Its usefulness also depends largely upon the fact that it is a convenient and relatively inexpensive source of these monosaccharides in cases where the presence of one does not interfere with the utilization of the other.

Invert sugar is sold commercially in liquid form (in some cases as a semisolid mass resulting from D-glucose crystallization), either alone or mixed with sucrose, under various trade names such as Flo-Sweet, Nulomoline, Liqua-Invert, and Cascade. It is also sold for pharmaceutical use as a 5 or 10% aqueous or saline solution (Solution Travert, N.N.R.). D-Glucose and D-fructose (derived from floral nectar) are widely distributed in honey, but not always in equimolecular proportion. Invert sugar is found in a wide variety of fruits and is probably the result, to a great extent, of hydrolysis of sucrose by the enzyme invertase or the naturally occurring acids of the fruits. The invertase enzymes, which are quite widespread throughout living cells, are of two kinds, an  $\alpha$ -glucosidase and a  $\beta$ -fructosidase (see Vol. 5, p. 759). The presence of invert sugar in substantial quantities has been reported in oranges, grapefruit, plums, cherries, apricots, peaches, tomatoes, mulberries, pomegranates, and numerous other fruits. It occurs in one type of dates (containing invertase) which are frequently called invert sugar dates. Invert sugar is found to only a small extent in sugar beets, although invertase is normally present in the beets and under certain conditions of soil and climate has been shown to produce small amounts of invert sugar (approximately 0.15% in the beet). The low invert sugar content in sugar beets facilitates the refining of beet sugar, since a high alkalinity may be maintained during processing to prevent further hydrolysis of sucrose without danger of forming the dark decomposition products resulting from the action of alkali on D-fructose. In the case of raw cane sugar, the presence of somewhat higher quantities of invert sugar prevents use of a high pH. Cane molasses contains considerable amounts of invert sugar. See also *Molasses*; *Sugar manufacture*.

**History (7).** It was early observed that when sucrose is heated with acid fruits graining of the sugar is prevented or considerably reduced. However, the name "invert sugar" was not applied to the mixture until Biot discovered in 1836 that the plane of polarized light passed through a sucrose solution was rotated to the right before heating with acids and to the left afterwards. Mitscherlich in 1843 found that strong inorganic and organic acids in concentrations between 0.01 and 0.10% would cause nearly complete inversion of sucrose. In 1847, Dubrunfaut separated D-glucose and D-fructose from a solution of sucrose which had been hydrolyzed with hydrochloric acid. Later, using tartaric, phosphoric, and oxalic acids in 0.01% concentration, Dubrunfaut obtained inversion of sucrose without the production of side reactions such as the formation of 5-(hydroxymethyl)furfural, levulinic acid or formic acid, which occurred with the use of strong mineral acids. Herzfeld in 1885 made a thorough study of inversion of sucrose and recommended the use of a 75% aqueous solution of sucrose with 0.11% tartaric acid maintained at a boiling temperature until it acquired a golden-yellow color. The resulting sirup was intended for blending with strong honeys to make them more palatable. He also recommended the use of invert sirups in making wine, in brewing, and in preserving those fruits deficient in acids.

#### PHYSICAL AND CHEMICAL PROPERTIES

As stated previously, the physical and chemical properties of invert sugar are those of an equimolecular mixture of D-glucose and D-fructose. Scheme 1 shows the formation of invert sugar from the hydrolysis of sucrose.



Invert sugar is almost always kept and used in liquid form since D-glucose crystallizes from the mixture more readily than D-fructose does. For this reason solubility

of invert sugar depends on the solubility of D-glucose in a D-fructose solution. Maximum solubility at 30°C. is 69.7% invert sugar (ref. 2, p. 362) (as compared with 68.11% for sucrose) at which concentration the solution is saturated with D-glucose. The solubility of invert sugar and of sucrose is reduced for each in the presence of the other, but the total sugar content in solution is increased. Thus a liquid sugar of maximum solubility at 30°C. contains 33.57% sucrose and 45.44% invert sugar (ref. 2, p. 365) for a total sugar content of 79.01%, and is saturated with sucrose and glucose.

Dried invert sugar absorbs water very rapidly, largely due again to the fructose moiety. Previously dried commercial invert sugar has been reported to absorb 5% moisture at 60% humidity in 9 days and 74% water in 25 days at 100% humidity (ref. 4, p. 7). Extrapolation of curves for mixtures of sucrose and invert sugar shows that a 20% mixture of invert sugar with sucrose will absorb about the same amount of water as that absorbed by a concentrated noncrystalline invert sugar sirup containing no sucrose (ref. 4, p. 9).

On the basis of sucrose as 100, invert sugar has been reported to have a sweetness of 85–130. The average value reported is about 105 (8). The specific rotation of invert sugar is dependent upon temperature as well as concentration; this is due principally to the fructose component of the mixture since the specific rotation of glucose is hardly affected by temperature (ref. 4, p. 472). Refractive indexes of invert sugar solutions at 20°C. have been reported (15). See also *Sugar analysis*, p. 193.

While sucrose is a nonreducing sugar, hydrolysis to invert sugar results in the formation of an aldehyde and a ketone group, both of which will reduce Fehling's solution. Only one osazone is formed from the invert sugar moieties, since both D-glucose and D-fructose yield glucosazone when heated with phenylhydrazine. Liquid invert sugar is most stable in color at about pH 3.3. At higher pH values a darkening effect takes place which is due to the degradation of the fructose component to complex products. In acid solution 5-(hydroxymethyl)furfural (see p. 258) is slowly formed.

#### ANALYSIS

Many methods exist for the determination of invert sugar either alone or in mixture with other sugars. Most of these methods depend upon reduction of copper compounds by the aldehyde and ketone groups of the sugars or upon polarization of the solution at two different temperatures. See also *Sugar analysis*.

The *copper reduction methods* most generally used are the Lane and Eynon or the Munson and Walker methods, both of which make use of the Soxhlet modification of Fehling's solution (2,4).

Since the specific rotation of D-fructose, and therefore that of invert sugar, has a high temperature coefficient, *polarization at two temperatures* is frequently used for the quantitative determination of invert sugar. The Gubbe formula for specific rotation of invert sugar can be solved for the temperature of complete inactivation. Browne (ref. 4, p. 473) has shown that this temperature varies with concentration from 83.2°C. for 2.0 grams to 90.2°C. for 60 grams per 100 ml. However, for practical purposes 87°C. is usually taken as the temperature of optical inactivity of invert sugar at any concentration. For this reason the difference between the direct polarizations at 20° and 87°C. is frequently used as a measure of the invert sugar present in a sample of mixed sugars.

Although the temperature of inactivity varies with concentration, the tempera-

ture coefficient of the rotation of invert sugar, reported as change in rotation per degree per gram per 100 ml., is independent of concentration and is equal to  $0.0180^\circ\text{V}$ . (degrees Ventzke) for each gram in 100 ml. Therefore, the invert sugar can be calculated from its polarization at any two widely different temperatures from the equation:

$$\frac{P' - P}{0.0180 (t' - t)} = \text{grams in 100 ml.}$$

where  $P'$  is the saccharimeter reading in degrees Ventzke at  $t'$ , and  $P$  the reading at  $t$  in a 2-dm. polarization tube.

*Other methods for determining invert sugar in the presence of sucrose* are the Herzfeld method (ref. 4, p. 806) for quantities of invert sugar less than 1.5% or the Meissl and Hiller method for mixtures in all proportions (ref. 4, p. 809) see also p. 197.

#### MANUFACTURE

The manufacture of invert sugar depends upon the hydrolysis of sucrose by one of three methods: (1) strong mineral or weak organic acids, (2) invertase, and (3) ion-exchange resins. While many patents exist for inversion they all depend on one of these hydrolysis reactions. Many of these patents are concerned with methods of rapid cooling or hydrolysis at a lower temperature to prevent secondary reactions resulting from heating at a low pH value.

*Hydrolysis with acid* has been, until recently, the practice for the manufacture of invert sugar on a commercial scale. A  $60^\circ$  Brix sucrose solution, which is brought to a pH of about 1.8 with hydrochloric acid, is usually employed at a temperature of approximately  $90^\circ\text{C}$ . Inversion is essentially complete in 30 minutes, after which the pH value is raised to 5.0–5.5 with dilute alkali. If it is desired, a sucrose solution can then be added to give the required mixture of sucrose and invert sugar. At the somewhat higher temperature of  $115^\circ\text{C}$ ., produced under a pressure of 10 p.s.i., inversion can be completed in 1 minute at a pH of 2.3.

*Hydrolysis with invertase* is used frequently for high-ash sugars where very large quantities of acid would be needed to overcome the buffering effect of these salts. A sucrose solution of  $45$ – $50^\circ$  Brix at a pH of 5.2–5.6 is kept at a temperature of  $55$ – $60^\circ\text{C}$ . in the presence of invertase until the desired degree of hydrolysis is obtained. Under these conditions approximately 95% inversion occurs in 24 hours. However, the hydrolysis can be stopped at any desired point by raising the temperature of the solution to  $70$ – $80^\circ\text{C}$ . in order to denature the invertase. Therefore, use of invertase is a convenient method where controlled hydrolysis is desirable.

*Hydrolysis with ion-exchange resins* is the most recent method of inversion (16). In this method a high-density sugar liquor, which has first been clarified and decolorized with carbon, is passed through a cation-exchange resin of the nuclear sulfonic type (see Vol. 8, p. 13) and the acidic effluent is held at approximately  $50^\circ\text{C}$ . until hydrolysis has proceeded to the required extent. The liquor is then passed through a weakly basic anion-exchange resin. The resulting product is a clear, water-white solution of sucrose and invert sugar stable in color, free of ash, and free of the decomposition products which originally marked the invert sugar made by acid inversion of sucrose at high temperatures.

High-test invert molasses is frequently produced from cheaper grades of cane juice. These solutions have a very high ash content. See *Molasses*, Vol. 9, p. 171.

**Economic Aspects.** In the U.S. during 1953 approximately 847,000 tons of sugar solids (sucrose and invert sugar) was sold in liquid form (see also *Sugar manufacture*, p. 226). About 30–40% of these solids was marketed as liquid invert sugar, the larger proportion of which consisted of liquid invert of maximum solubility. The remainder of the liquid invert sugar consisted of total invert sugar (completely inverted) or custom-made blends of sucrose and invert sugar. The steady increase in tonnage of sugar solids in liquid form from 300,000 tons in 1947 to 847,000 tons in 1953 indicates the acceptance by more and more industrial users of the convenience, sanitation, and savings which the bulk handling of liquid sugar under certain conditions provides to industry. Liquid invert sugar sales have been increasing continuously since the introduction of the ion-exchange method of inversion.

#### USES

Properties such as moisture retention, high degree of sweetness, and high solubility of the D-fructose component, and retardation of crystallization of sucrose in mixture contribute to the value of invert sugar for various food uses.

In confectionery (*q.v.*), invert sugar is used to restrict the tendency of candy to dry out and crystallize on standing. In fondant candies, including those with embedded fruits, softened or even completely liquefied centers are often produced by addition of the enzyme invertase to the fondant, resulting in a slow inversion of sucrose. Addition of invertase to chocolate-coated fondant, candy ("hand-rolled creams") prevents fermentation and bursting by inverting part of the sucrose. The candy is thereby made resistant to yeast action since the density and osmotic pressure of the sirup in the fondant are increased (10). Invert sugar is also utilized in the preparation of jellies and preserved fruits where inversion of sucrose takes place during the cooking process due to hydrolysis by fruit acids. It is this inversion that prevents rapid graining of preserves. Commercial liquid invert sugar is used by commercial manufacturers of jams and jellies, by the canning industry, and by producers of carbonated beverages (*q.v.*). The extent of its substitution for sucrose in ice cream is limited by the lowered freezing point of the final product.

The baking industry (see Vol. 2, p. 279) has successfully employed invert sugar to keep the products soft and prevent cracking. In Austria and Germany at the time of World War I its use was advocated to replace up to 5% of the flour and as a substitute for more difficultly obtainable fats. Satisfactory or even superior loaves of bread were formed if the salt content was increased to overcome the additional sweetness (3,6).

The use of liquid invert sugar has been advocated in place of simple sirup in pharmaceutical preparations (13). Medicinally, invert sugar has found its most important use for intravenous injections (17), where it has proved efficacious in general use and particularly under certain pathological conditions such as diabetes (9). Invert sugar solution is more easily prepared than D-glucose solution and may be retained to a slightly greater extent. In infant and invalid feeding it is more easily absorbed than maltose, lactose, or sucrose. It produces more effective deposition of glycogen in the liver of rats than does either D-glucose or D-fructose alone even in cases where severe liver damage exists (5). It has been suggested as a sclerosing agent in the treatment of varicose veins (12).

Invert sugar is used by the tobacco (*q.v.*) industry as a humectant to control the moisture content of prepared tobaccos. The hygroscopicity of invert sugar has also led to its use in the plasticizing of paper, and its application in the treatment of timber

and wooden products has been proposed to prevent drying out and warping. The possible advantages of invert sugar as a humectant have been discussed by Andersen (1), taking into consideration the availability, relative prices, and amounts needed.

### Bibliography for Invert Sugar

- (1) Andersen, W., *Svensk. Papperstidn.*, **55**, 181 (1952).
- (2) Bates, F. J., *et al.*, "Polarimetry, Saccharimetry and the Sugars," *Natl. Bur. Standards (U.S.), Circ.*, **C440** (1942).
- (3) Baudrexel, A., *Deut. Zuckerind.*, **40**, 320 (1915).
- (4) Browne, C. A., and Zerban, F. W., *Physical and Chemical Methods of Sugar Analysis*, 3rd ed., Wiley, N.Y., 1941.
- (5) Gerlich, N., and Remy, R., *Deut. Z. Verdauungs. u. Stoffwechselkrankh. Sonderband*, 67 (1952).
- (6) Jelinek, J., *Z. Zuckerind. Böhmen.*, **39**, 281 (1915).
- (7) Jordan, S., *Ind. Eng. Chem.*, **16**, 307 (1924).
- (8) Miller, W. T., *Food Packer*, **27**, No. 13, 50, 54 (1946).
- (8a) Neuberg, C., and Roberts, I. S., *Invertase*, Sugar Research Foundation, N.Y., 1946.
- (9) *Nutrition Rev.*, **11**, No. 10, 299 (1953).
- (10) Paine, H. S., Birkner, V., and Hamilton, J., *Ind. Eng. Chem.*, **19**, 358 (1927).
- (11) Rannels, K., *Automotive and Aviation Inds.*, **98**, No. 7, 25 (1948).
- (12) Rees, H. C., *Grace Hosp. Detroit Bull.*, **22**, 1 (1938).
- (13) Whatmaugh, W. A., *Pharm. J.*, **118**, 724, 789 (1927); *Chemist & Druggist*, **107**, 18, 115 (1927).
- (14) Zerban, F. W., *J. Am. Chem. Soc.*, **47**, 1104 (1925).
- (15) Zerban, F. W., and Martin, J. J., *J. Assoc. Offic. Agr. Chemists*, **27**, 295 (1944).
- (16) U.S. Pat. 2,594,440 (April 29, 1952), M. F. Hughes, M. McCalip, H. S. Paine, and N. Rosenberg (to Refined Syrups & Sugars, Inc.).
- (17) Brit. Pat. 687,668 (Feb. 18, 1953), Sugar Research Foundation, Inc.

LOUISE L. PHILLIPS AND MARY F. HUGHES

### D-Fructose

D-Fructose (fructose, levulose, fruit sugar),  $C_6H_{12}O_6$ , formula weight 180.16, is a white crystalline ketohexose. It is commercially available as crystals in pilot plant quantities and as a 10% aqueous solution (Levugen, N.N.R.). In the U.S., interest in fructose has been aroused during recent years because of new knowledge concerning its medical usefulness when administered intravenously.

D-Fructose exists widely in nature, but until recently it has been considered among the rare sugars owing to the difficulty of obtaining it in its free form. Its enantiomorph, L-fructose, does not occur naturally but has been prepared synthetically (30). D-Fructose is found in the free state in honey and fruits and is the only carbohydrate in human and bull semen. Recently it has been found in low concentration (2-6 mg./100 ml.) in human blood but in higher concentration in placental and fetal blood (6). D-Fructose is found combined in the disaccharide sucrose, in oligosaccharides such as raffinose, stachyose, verbascose, and in many carbohydrate polymers known as *fructans* (fructosans) and *levans* (1). A large number of fructans occur in roots, stems, seeds, and leaves of various plants such as the dahlia, Canadian thistle, chicory, and Jerusalem artichoke (27). The levans are produced from sucrose or raffinose by many types of bacteria. See also *Polysaccharides*.

Harding (7) and McGlumphy and Eichinger (15) have reviewed the interesting historical aspects of this sugar. In 1843, Crookewitt hydrolyzed the fructan inulin, and obtained an "uncrystallizable sugar." That same year Soubeiran hydrolyzed



sucrose and observed that dextrose (*q.v.*) was not the sole product of hydrolysis. This finding was confirmed by Dubrunfant and, after further study, he reported in 1856 that invert sugar consisted of two sugars, D-glucose and a second sugar identical with the one obtained from inulin. In 1880, this hitherto uncrystallizable sugar obtained from sucrose was crystallized by Jungfleisch and Lefranc, and in the same year Kiliani successfully crystallized fructose obtained by hydrolysis of inulin. Within the next ten years the structure of D-fructose was established by Kiliani and Fischer. Since that time, numerous attempts have been made to develop an economical, efficient method for the production of D-fructose. Recent developments indicate that some success is being made in that direction. See also "Invert Sugar."

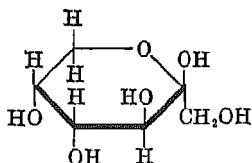
#### PHYSICAL AND CHEMICAL PROPERTIES

D-Fructose is considered to be the most soluble and the sweetest of the sugars. It is exceedingly soluble in water but only slightly soluble in absolute ethyl alcohol. For complete information on the solubility of D-fructose and its refractive index in aqueous solutions see reference (2), pp. 670, 681-89. Its sweetness is dependent upon concentration; in 4.5-16.7% solutions it is 1.1-1.2 times as sweet as sucrose (4). The sweetness is also affected by temperature (see p. 248).

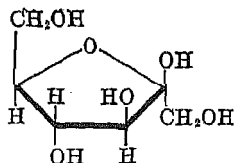
D-Fructose crystallizes from alcoholic solution in anhydrous form as small colorless prisms, m.p. 102-4°C. Crystallization from cold concentrated aqueous solution frequently results in spherulitic aggregates of fine needles of D-fructose hemihydrate. Above 20°C., D-fructose hemihydrate changes slowly into the stable anhydrous form (12).

In a study of the D-fructose-water system, Young and colleagues (26) demonstrated the existence of three crystalline phases of D-fructose: the anhydrous, hemihydrate, and dihydrate forms. Crystals of both anhydrous D-fructose (ref. 2, p. 543) and D-fructose dihydrate (26) are described as follows: crystal system—orthorhombic; class 6—rhombic bisphenoidal; habit—prismatic. D-Fructose hemihydrate (12) belongs to the hexagonal crystal system and exists as rods or needles. D-Fructose dihydrate and a process for its preparation have been patented (34).

The specific rotation of a freshly prepared solution of D-fructose at 20°C. and 4 g./100 ml. solution changes rapidly, from -132° to -92.4°. This mutarotation is due to the establishment of equilibrium between the pyranose (V) and furanose (VI) structures (8), since there apparently is no equilibrium between  $\alpha$ - and  $\beta$ -forms, only the  $\beta$ -form being known (see p. 229). At 25°C. an aqueous solution of D-fructose contains about 22%  $\beta$ -D-fructofuranose (VI) (5). The effect of temperature and concentration on the specific rotation of D-fructose has been studied by Tsuzuki *et al.*



(V)  $\beta$ -D-Fructopyranose



(VI)  $\beta$ -D-Fructofuranose

(24,25) and may be summarized for the range of  $p = 5-40$  and  $t = 10-90$  by the equation:

$$[\alpha]_D^t = - (103.6 + 0.134p) + (0.59 + 0.0003p)t$$

where  $p$  is per cent concentration by weight and  $t$  is temperature Centigrade.

The structure of crystalline D-fructose is  $\beta$ -D-fructopyranose (V), but in combined form (sucrose, inulin, etc.) the fructose units possess the furanose ring (VI).

D-Fructose seems to be less stable than D-glucose, both in the crystalline state and in solution. The colorless crystals are slightly hygroscopic and on long exposure to air undergo gradual decomposition, as is evident by appearance of yellow to tan coloration. In aqueous solution, the stability of D-fructose is dependent upon temperature, pH, and the presence of oxygen. In an exhaustive study of this problem Mathews and Jackson (14) found maximum stability to be at pH 3.3 regardless of temperature.

In mildly alkaline solution, D-fructose undergoes the Lobry de Bruyn-Alberda van Ekenstein rearrangement (see p. 238). In strongly alkaline solution, destruction is rapid with formation of a complex mixture of decomposition and rearrangement products.

In acid solution, fructose is slowly dehydrated to 5-(hydroxymethyl)furfural,  $\text{HO}-\text{H}_2\text{CC}:\text{CH}:\text{CH}:\text{CCHO}$ , which in turn polymerizes to colored substances responsible

for the gradual darkening of aqueous solutions of fructose. On standing, these solutions also develop 5-(hydroxymethyl)furoic acid, presumably from the oxidation of 5-(hydroxymethyl)furfural (23). When acid solutions of fructose are boiled for several hours, condensation of fructose occurs to a slight degree with the formation of *difructose dianhydrides* (diheterolevulosans) (20). Wolfrom, Hilton, and Binkley (29) have isolated and identified five dianhydrides formed by the action of concentrated hydrochloric acid on D-fructose.

The behavior of D-fructose both in alkaline and in acid solutions has an important bearing on the successful preparation of pure D-fructose.

Numerous derivatives of D-fructose such as phosphates, organic esters, and ethers have been prepared (1).

#### ANALYSIS

There are numerous methods available for the determination of D-fructose in the presence of other sugars or nonsugars (1,22). Only the more widely used methods will be considered here. See also *Sugar analysis*.

In the presence of optically inactive substances (3) the amount of D-fructose as grams/100 ml. (c) in a solution may be calculated from the angular rotation (a) in *levo* degrees measured at 20°C. in a 2-dm. polarimeter tube using the equation:

$$c = \frac{100a}{2(-92.5)} = -0.5405a$$

(-92.5 is the specific rotation of D-fructose at 20°C.). The specific rotation of D-fructose changes markedly with change of temperature, whereas the rotations of D-glucose and sucrose do not. Therefore, by measuring the rotation at different temperatures an empirical relationship has been developed for estimating D-fructose in the presence of D-glucose and sucrose (ref. 2, pp. 217-18). The so-called Mathews formula (10) is often used for determination of D-fructose and D-glucose in mixtures containing the two sugars only. In the method, polarization and total reducing sugar (Lane and Eynon method—p. 197) are measured and the concentrations then calculated by tables compiled by Mathews.

One of the chief colorimetric methods is based on the blue color which diphenyl-

amine gives with 5-(hydroxymethyl)furfural formed when D-fructose is heated in the presence of strong acids (17). It is applicable to determination of fructose in blood and urine (13). Under the conditions of the analysis, D-glucose will give little color as compared to D-fructose, for example, 1 mg. of D-fructose produces as much color as 14-25 mg. of D-glucose. Another colorimetric method, using resorcinol instead of diphenylamine, was developed by Roe (18) for determining D-fructose in blood and urine, but the method can be used also for analysis of other D-fructose-containing solutions.

Recently, Wise and colleagues (28) described a method for determining traces of D-fructose liberated by hydrolysis of various dextrans. After acid hydrolysis, the D-fructose and D-glucose units are separated from the polysaccharides on a paper chromatogram and, after elution, the amount of D-fructose in the D-fructose-D-glucose spot is determined quantitatively by a modification of the anthrone method (21). This method should be applicable to the analysis of many materials containing D-fructose in free or bound form.

#### MANUFACTURE

At this time, there is no accepted, well-standardized procedure for manufacturing D-fructose, but as a result of several investigations it now appears that D-fructose can be manufactured in large enough quantity and at low enough cost to supply any demand for it that may arise.

The two major sources from which D-fructose has been obtained are the Jerusalem artichoke (*Helianthus tuberosus* L.) and sucrose. The Hawaiian ti plant also appears to be a potential source of D-fructose. According to the literature, the most promising methods for isolating pure D-fructose involve modifications and improvements of the original discovery made over 100 years ago by Dubrunfaut for separating fructose from glucose. Briefly the methods involve hydrolysis of the juices from tubers of the Jerusalem artichoke or of sucrose, separation of fructose as an insoluble lime-fructose complex ( $C_6H_{12}O_6 \cdot CaO$ ), liberation of fructose by acidification of the complex with acids that form insoluble calcium salts (such as carbonic or phosphoric acid), removal of cation and anion contaminants by means of cation- and anion-exchange resins (such as Duolite C-3 and Duolite A-3), concentration of the resulting fructose solution to a thick sirup *in vacuo*, and finally crystallization of D-fructose. However, for the successful accomplishment of these apparently simple operations certain reaction conditions must be met. The most important conditions are operation at low temperature and avoidance of excessive acidity or alkalinity throughout the entire procedure.

The most extensive studies on the production of D-fructose by hydrolysis of the polysaccharides extracted from the Jerusalem artichoke have been made by McGlumphy *et al.* (15,31) at Iowa State College and by Jackson *et al.* (9,11,32) at the National Bureau of Standards. Although on the basis of these fundamental studies a semicommercial plant was built at the Bureau with an estimated production capacity of about 1000 lb. of D-fructose per day, the operation was not continued chiefly because the Jerusalem artichoke is not a crop plant in the U.S. The fructose-bearing polymers, inulin, inulenin, and synanthin, are stored in the tubers of the plant and harvesting the tubers is relatively costly. Furthermore, the tubers must be collected and processed at the correct time for maximum yield of D-fructose, and this fact tends to make the

process a seasonal operation. The investigators at Iowa State College partially overcame this disadvantage by developing a method of slicing the tubers and dehydrating the chips to eliminate loss of fructose on storage.

Sucrose therefore appears to be a more feasible source of *D*-fructose than the Jerusalem artichoke. In 1944, the Sugar Research Foundation granted funds to the Department of Chemical Engineering of the University of Colorado for investigating the possibility of large-scale production of *D*-fructose from sucrose. An almost continuous process for producing *D*-fructose from sucrose was developed by this effort (19,22). In 1951, this group of investigators estimated that *D*-fructose could be produced from refined sugar for about 65¢ per pound. The purity of the *D*-fructose prepared by them was remarkably high, 98.6-100%. The use of cation- and anion-exchange resins not available to the earlier investigators contributed much toward the attainment of such high purity.

Several methods of separating *D*-glucose from invert sugar (see p. 251), leaving *D*-fructose, have been attempted, such as formation of insoluble benzidine derivatives of *D*-glucose and sodium chloride addition compounds of *D*-glucose, but these have not been practicable. Fructose has been made on a small scale from invert sugar by oxidation of the glucose (33). *D*-Fructose remains as a by-product during the bacterial production of dextran (a plasma expander (*q.v.*)) from sucrose, and one firm is investigating this as a possible source of the sugar.

**Economic Aspects.** Five companies in the United States (Mead Johnson & Company, Pfauastiehl Chemical Company, R. K. Laros Company, Holly Sugar Corporation, and Abbott Laboratories) are producing *D*-fructose on a pilot-plant scale. All will probably go into large-scale production if the demand for *D*-fructose should warrant that action. What the annual demand will be is still unknown, but estimates of 200,000-360,000 lb. have been made, which is small by comparison with the production of dextrose and sucrose.

In 1926, the price of *D*-fructose was \$30-110 per pound and it was available only in ounce quantities. In May 1954, it was being sold for \$4.00 per pound, with the probability that it will be sold at less than half this figure when it is produced in large quantities.

#### USES

Until recently the use of *D*-fructose in its pure form has been exceedingly limited because of its high cost and unavailability. Actually as a component of invert sirups and honey it has been used extensively for a long time by the baking, candy, and food industries. It has been estimated that the U.S. consumes over six billion pounds of *D*-fructose annually in these forms.

At present its chief and most promising use in pure form is as a source of calories for patients who must be fed intravenously. Under conditions of stress such as surgery, starvation, and diabetes, *D*-fructose administered intravenously is utilized normally whereas *D*-glucose is not. Other advantages of *D*-fructose over *D*-glucose are a more adequate provision of calories, as a result of less loss of sugar (calories) in the urine and a shorter infusion time (with consequently less discomfort to the patient), and a more rapid formation of liver glycogen (16). Early in 1953, the first solution of *D*-fructose (Levugen, N.N.R.) designed for intravenous administration became available in the U.S.

## Bibliography for D-Fructose

- (1) Barry, C. P., and Honeyman, J., "Fructose and Its Derivatives" in *Advances in Carbohydrate Chemistry*, Academic Press, N.Y., 1952, Vol. VII, pp. 53-98.
- (2) Bates, F. J., *et al.*, "Polarimetry, Saccharimetry and the Sugars," *Natl. Bur. Standards (U.S.), Circ.*, C440 (1942).
- (3) Browne, C. A., and Zerban, F. W., *Physical and Chemical Methods of Sugar Analysis*, 3rd ed., Wiley, N.Y., 1941, p. 294.
- (4) Dahlberg, A. C., and Penczek, E. S., *The Relative Sweetness of Sugars as Affected by Concentration* (Tech. Bull. No. 258), N.Y. State Agricultural Expt. Sta., Geneva, N.Y., 1941.
- (5) Gottschalk, A., *Nature*, **156**, 540-41 (1945).
- (6) Hagerman, D. D., and Vilee, C. A., *J. Clin. Invest.*, **31**, 911-13 (1952).
- (7) Harding, T. S., *Sugar*, **25**, 406-8 (1923).
- (8) Isbell, H. S., and Pigman, W. W., *Bur. Standards J. Research*, **20**, 773-98 (1938).
- (9) Jackson, R. F., Silsbee, C. G., and Proffitt, M., *J. Bur. Standards Sci. Paper*, **20**, No. 519, 587-619 (1926).
- (10) Jackson, R. F., and Mathews, J. A., *Bur. Standards J. Research*, **8**, 433 (1932).
- (11) Jackson, R. F., and Mathews, J. A., *Bur. Standards J. Research*, **15**, 341-56 (1935).
- (12) Jones, F. T., Young, E. E., and Black, D. R., *Anal. Chem.*, **25**, 649 (1953).
- (13) Martin, R. W., *Z. physiol. Chem.*, **259**, 62-74 (1939).
- (14) Mathews, J. A., and Jackson, R. F., *Bur. Standards J. Research*, **11**, 619-33 (1933).
- (15) McGlumphy, J. H., and Eichinger, J. W., Jr., *J. Chem. Educ.*, **10**, 453-63 (1933).
- (16) *Nutrition Rev.*, **11**, 299-301 (Oct. 1953).
- (17) Oppel, W. W., *Biochem. Z.*, **229**, 85-99 (1930).
- (18) Roe, J. H., *J. Biol. Chem.*, **107**, 15-22 (1934).
- (19) Rohrman, F. A., *Sugar J.*, **13**, 10-11, 18 (1950).
- (20) Sattler, L., Zerban, F. W., Clark, G. L., Chu, C., Albon, N., Gross, D., and de Whalley, H. C. S., *Ind. Eng. Chem.*, **44**, 1127-35 (1952).
- (21) Scott, T. A., and Melvin, E. H., *Anal. Chem.* (in press).
- (22) Sugar Research Foundation, *The Pilot Plant Production of Levulose (D-Fructose)* (Member Rept. No. 29), December 1951.
- (23) Turner, J. H., Rebers, P. A., Barrick, P. L., and Cotton, R. H., "Notes on the Determination of Hydroxymethylfurfural and Related Compounds," *Abstracts of Papers, 124th Meeting Am. Chem. Soc. (Chicago)*, Sept. 1953, p. 8D.
- (24) Tsuzuki, Y., Yamazaki, J., and Kagami, K., *J. Am. Chem. Soc.*, **72**, 1071-73 (1950).
- (25) Tsuzuki, Y., and Yamazaki, J., *J. Am. Chem. Soc.*, **74**, 3237-38 (1952).
- (26) Young, F. E., Jones, F. T., and Lewis, H. J., *J. Phys. Chem.*, **56**, 738-39, 1093-96 (1952).
- (27) Whistler, R. L., and Smart, C. L., *Polysaccharide Chemistry*, Academic Press, N.Y., 1953, ch. 11.
- (28) Wise, C. S., Dimler, R. J., Davis, H. A., and Rist, C. E., "Determination of Easily Hydrolyzable Fructose Units in Dextran Preparations," *Abstracts of Papers, 124th Meeting Am. Chem. Soc. (Chicago)*, Sept. 1953, p. 2D.
- (29) Wolfrom, M. L., Hilton, H. W., and Binkley, W. W., *J. Am. Chem. Soc.*, **74**, 2867-70 (1952).
- (30) Wolfrom, M. L., and Thompson, A., *J. Am. Chem. Soc.*, **68**, 791-93 (1946).
- (31) U.S. Pat. 1,970,605 (Aug. 21, 1934), R. M. Hixon, J. H. McGlumphy, J. W. Eichinger, Jr., and J. H. Buchanan (to Iowa State College).
- (32) U.S. Pat. 2,007,971 (July 16, 1935), R. F. Jackson (to U.S.A.).
- (33) U.S. Pat. 2,567,060 (Sept. 4, 1951), G. C. Docal (to Sugar Research Foundation).
- (34) U.S. Pat. 2,588,449 (March 11, 1952), F. E. Young and F. T. Jones (to U.S.A.).

R. C. ELLINGSON

## SUGAR DERIVATIVES

There are many kinds of substances that may be considered to be derivatives of sugars. Among the naturally occurring derivatives are sugar alcohols (see *Alcohols, higher polyhydric*), sugar acids (see Table I), glycosides (see *Cardiovascular agents*;

*Glycosides*), and polysaccharides (*q.v.*). Derivatives that are manufactured may be arbitrarily divided into those formed by degradation and those formed by combining reactions.

### Degradation Products

The many degraded products may be subdivided into those produced by fermentation and by chemical degradations.

TABLE I. Naturally Occurring Sugar Acids.

Structure	Name	Natural source
$  \begin{array}{c}  \text{CHO} \\    \\  \text{HCOH} \\    \\  \text{HOCH} \\    \\  \text{HOCH} \\    \\  \text{HCOH} \\    \\  \text{COOH}  \end{array}  $	D-Galacturonic acid	Combined in pectins, karaya gum, and gum. tragacanth.
$  \begin{array}{c}  \text{CHO} \\    \\  \text{HOCH} \\    \\  \text{HOCH} \\    \\  \text{HCOH} \\    \\  \text{HCOH} \\    \\  \text{COOH}  \end{array}  $	D-Mannuronic acid	Combined in alginic acid.
$  \begin{array}{c}  \text{CHO} \\    \\  \text{HCOH} \\    \\  \text{HOCH} \\    \\  \text{HCOH} \\    \\  \text{HCOH} \\    \\  \text{COOH}  \end{array}  $	D-Glucuronic acid	Combined in animal urine, pneumococcus type III polysaccharide, hyaluronic acid, chondroitinsulfuric acid, heparin, mesquite gum, and gum arabic.
$  \begin{array}{c}  \text{COOH} \\    \\  \text{C=O} \\    \\  \text{HOCH} \\    \\  \text{HCOH} \\    \\  \text{HCOH} \\    \\  \text{CH}_2\text{OH}  \end{array}  $	2-Keto-D-gluconic acid	Combined in carageenin, the polysaccharide of Irish moss ( <i>Chondrus crispus</i> ).

### FERMENTATION DEGRADATION

Fermentation of sugars and other carbohydrates leads to a wide variety of products ranging from carbon dioxide to antibiotics to yeasts. Several fermentive reactions have been the source of organic chemicals of considerable industrial significance, such as acetone and 1-butanol. However, except for potable ethyl alcohol, and

citric, gluconic, and lactic acids, production from petroleum or electrochemical methods have for the most part supplanted the fermentation processes. Many other substances have been reported to be products of fermentation reactions (4). See also *Fermentation*.

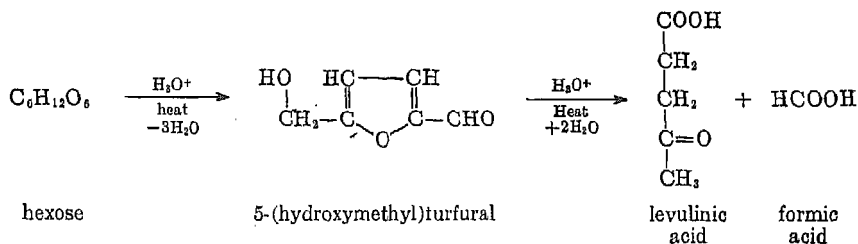
#### CHEMICAL DEGRADATION

Sucrose dextrose, and lactose, when heated, lose water and darken in color. The product is caramel (*q.v.*), which is useful for coloring and flavoring foods and beverages. More severe thermal degradation in the presence of acids produces furfural (*q.v.*) from pentose sugars and aldohexuronic acids. This degradation is performed on a large scale with pentosan-containing raw materials such as corn cobs. Hexose sugars by the same treatment yield 5-(hydroxymethyl)furfural, which upon further degradation produces levulinic acid.

Sucrose, when heated in the presence of calcium hydroxide, degrades and rearranges to yield a variety of products, including lactic acid (*q.v.*) and the saccharinic acids. See also pp. 238, 250.

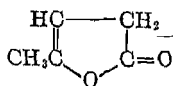
Dextrins, in which part of the sugar residues are dehydrated, are obtained by thermal degradation of starch (*q.v.*).

**Levulinic acid**,  $\text{CH}_3\text{CO}(\text{CH}_2)_2\text{COOH}$ , formula weight 100.11, small colorless leaflets, m.p.  $37.2^\circ\text{C}$ .,  $d_4^{20}$  1.1395, is very soluble in water, ethyl alcohol, and ether. It is produced along with formic acid when a hexose sugar is heated in the presence of oxalic acid or a mineral acid, decomposing in several steps of dehydration and degradation:

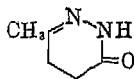


A process has been reported which gives a 70% conversion of a 3% sucrose solution. One manufacturer produces levulinic acid from corn starch in about 50% yield. It is also a by-product of furfural production.

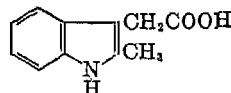
Several heterocyclic compounds (such as I, II, and III) have been prepared from levulinic acid, but none have provided a significant outlet for the consumption of levulinic acid, although calcium levulinate may be used medicinally as a source of calcium. In general, the production potential of levulinic acid greatly exceeds the demand at present high prices.



(I)  $\alpha$ -Angelica lactone



(II) 3-Methyl-6-ketotetrahydropyridazine  
(6-methyl-4,5-dihydro-3(2H)-pyridazinone)



(III) 2-Methyl-3-indole-acetic acid

### Products of Combining Reactions

Few sugar derivatives outside of the degradative derivatives have attained any sizable market. Two important hydrogenation products, sorbitol and mannitol (see *Alcohols, higher polyhydric*) are useful as humectants and can be converted to other useful products including surface-active agents and alkyd-type resins. Mannitol forms the primary explosive mannitol hexanitrate (see Vol. 6, p. 34). Dextran (see *Plasma expanders; Polysaccharides*) is being produced from sucrose fermentation on a large scale.

### ESTER DERIVATIVES

The essentially hydrophilic character of sugar can be modified (that is, usually reduced) to a degree dependent upon the type and number of acid groups introduced. At the same time a considerable change in other properties occurs. For example, sucrose, one of the sweeter of the natural products, becomes exceedingly bitter when acetylated. Some of the esters of sucrose are listed in Table II. This list does not include the large number of partially esterified products. Maltose octapropionate is one of the best crystallized derivatives of maltose. In contrast to the unsubstituted sugars, the acetates and propionates of mono- and disaccharides are distillable at 0.001 mm. Hg.

TABLE II. Totally Esterified Sucrose Esters.

Ester	Mol. Wt.	M.p., °C.
Acetate.....	678.59	72.3
Propionate.....	790.80	44-46
Palmitate.....	2249.50	54-55
Stearate.....	2473.92	57
<i>p</i> -Nitrobenzoate.....	1537.13	150 (d.)
<i>p</i> -Bromobenzoate.....	1135.89	114-117
Cinnamate.....	1385.42	87-88
Nitrate.....	704.32	85.5

Nitrate esters of sugars have received repeated attention as explosives, but they are less stable than the nitrates of glycerol and the sugar alcohols. Lactose octanitrate and, to a lesser extent, sucrose octanitrate have found use when glycerol was in short supply, but they do not compete on a free market.

Phosphate esters are intermediates in sugar metabolism and *in-vivo* synthesis of carbohydrates.

The hydrophilic character of some sugar derivatives has suggested their use in surface-active agents. Examples of derivatives proposed for use as wetting agents are di-*O*-lauroyl-*D*-glucosyl sulfate (12) and sugar phosphate dioleate (9). *N*-Cetyl-*N*-methylglucamine (11) and *N*-cetyl-*N*-*D*-glucosyl-*N*-methylammonium iodide (10) are among those suggested as emulsifiers. The esters of sucrose formed by reaction with the acid chlorides of China wood or perilla oils are drying oils. Some success has also been achieved with corresponding derivatives of linseed oil.

**Acetates.** Franchimont, in 1879, reacted sodium acetate and acetic anhydride with *D*-glucose. With but slight modifications, this is the currently recommended method for preparing acetates. The reaction is general for sugars and carbohydrates. Other reagents which have been recommended include: acetic anhydride and pyridine,



acetic anhydride and sulfuric acid, and acetic anhydride and zinc chloride. As a rule, mild reagents and low temperatures (below 50°C.) favor the  $\alpha$ -configuration if the  $\alpha$ -form is taken at the outset, while high temperatures (100–130°C.) and stronger catalysts favor the  $\beta$ -derivatives regardless of the original configuration. In intermediate ranges, mixtures result.

The acetates have been of particular importance to the carbohydrate chemist. They frequently will crystallize, forming derivatives whose properties usually are regular. Acetates of the glucose, cellobiose, etc., series demonstrate this order (see Table III) (3).

TABLE III. Acetates of Cellobiose-Type Sugars.

Acetate	M.p., °C.	$[\alpha]_D^{20}$ (CHCl <sub>3</sub> , c > 5)
$\alpha$ -D-Glucopyranose pentaacetate	113	+ 101.6°
$\alpha$ -Cellobiose octaacetate	229	+ 41.0
$\alpha$ -Cellotriose hendecaacetate	223–24	+ 22.6
$\alpha$ -Cellotetraose tetradecaacetate	230–34	+ 13.4
$\alpha$ -Cellopentaose heptadecaacetate	240–41	+ 4.17
$\alpha$ -Cellohexaose eicosaacetate	252–55	– 0.23

*Sucrose octaacetate*, C<sub>12</sub>H<sub>14</sub>O<sub>11</sub>(C<sub>2</sub>H<sub>3</sub>O)<sub>8</sub>, formula weight 678.59, white needles from alcohol, m.p. 72.3°C.,  $[\alpha]_D^{22}$  +59.6° (CHCl<sub>3</sub>), is soluble in ethyl alcohol, ether, and common organic solvents, and very slightly soluble in water. It is the only sucrose derivative having any considerable commercial production. The octaacetate is prepared with sodium acetate and acetic anhydride by the Franchimont method. Sucrose octaacetate is commercially available in 100–200-lb. bags and in July, 1954, was selling at \$0.76/lb.

About twenty tons of the acetate is consumed annually in denaturing ethyl alcohol. The compound imparts an exceedingly bitter taste to the alcohol but is nontoxic. Mixed with glucose pentaacetate, it finds use as an adhesive, as does sucrose-modified polyvinyl alcohol. These materials have achieved some use in laminated glass. Sucrose octaacetate is also used as a plasticizer in dialkyl succinate and maleic anhydride-styrene resins. In phenol-formaldehyde or phenol-furfural polymers, it produces a plastic particularly useful in bonding asbestos brake linings.

#### ACID DERIVATIVES

Of the many sugar acids (glyconic, glycuronic, and glycaric) only the most important are described here. For other acids, such as citric, lactic, fumaric, and itaconic, that can be obtained from sugars see *Fermentation* and the articles on the acids.

**D-Gluconic acid**, C<sub>6</sub>H<sub>12</sub>O<sub>7</sub>, formula weight, 196.16, fine needles, m.p. 125–26°C.,  $[\alpha]_D^{20}$  –6.7°  $\rightarrow$  +11.5° (H<sub>2</sub>O, c = 5); is soluble in water and insoluble in ethyl alcohol and ether. No natural source has been reported for D-gluconic acid, but, because its salts have been of interest, some has been prepared by aerobic fermentation of D-glucose. In shallow pans, *Penicillium chrysogenum* will give a 60% conversion in 8–10 days. *Aspergillus niger* NRRL 3 or 67 in rotating fermenting drums is said to give a 95% conversion if boric acid is added to complex the D-gluconic acid as it is formed. D-Gluconic acid is usually prepared by aerobic fermentation of D-glucose with *Acetobacter suboxydans*. It may also be prepared in good yield by electrolytic oxidation (4a). See *Electrosynthesis, organic*, Vol. 5, p. 667.

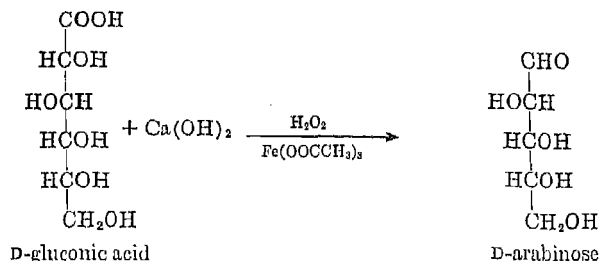
The acid of commerce is a 50% aqueous solution (7). In July, 1954, the acid was selling for \$0.15½ to 0.35/lb. in drum lots or less. *Sodium gluconate* is available in both the technical and refined grades and in July, 1954, was selling for \$0.35 and 0.83/lb. *Calcium gluconate* in barrels or drums sold for \$0.63–0.65/lb. (U.S.P.) and for \$0.70–0.72/lb. (AA) in July, 1954, and *potassium gluconate* sold for \$0.75–0.79/lb. in drum lots. The potassium salt is also available as a solution for intravenous use selling at \$0.67/lb.

Gluconic acid is used in cleaning metal containers, particularly in the dairy industry to remove milkstone. Salts of D-gluconic acid have found interest in pharmacy as a means of administering calcium or iron (see Table IV). The sodium salt in the presence of caustic alkali is a sequestrant for iron or calcium as in boiler water conditioning. It is claimed to be superior to sodium citrate or tetrasodium ethylenediaminetetraacetate (2,14). See also "Hydroxy Carboxylic Acids" under *Sequestering agents*.

TABLE IV. Salts of D-Gluconic Acid.

Salt	Appearance	M.p., °C.	Solubility
Ammonium	Fine, white needles	154 (dec.)	31.6 g./100 ml. H <sub>2</sub> O/25°; s.l.s. EtOH; i. organic solvents
Sodium	Irregular, colorless	—	59 g./100 ml. H <sub>2</sub> O/25°; i. organic solvents
Potassium	Fine, white cryst. powder	dec. 180	Readily s. H <sub>2</sub> O
Calcium	Fine, white needles	—	3.5 g./100 ml. H <sub>2</sub> O/25°; i. Et <sub>2</sub> O, EtOH
Magnesium, monohydrate	White powder	—	10.6 g./100 ml. H <sub>2</sub> O/25°; i. organic solvents
Ferrous, monohydrate	Fine, yellowish-green powder	—	8.5 g./100 ml. H <sub>2</sub> O/100°; s.l.s. EtOH; i. Et <sub>2</sub> O (solutions are reduced by light owing to a photochemical reaction) (see Vol. 8, p. 69)
Cupric	Light bluish-green	—	30 g./100 ml. H <sub>2</sub> O/25°; i. organic solvents

Another use proposed for D-gluconic acid involves a Ruff degradation of the calcium salt to D-arabinose:



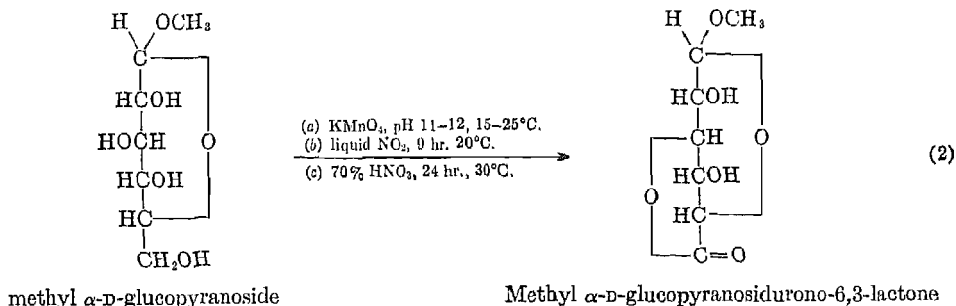
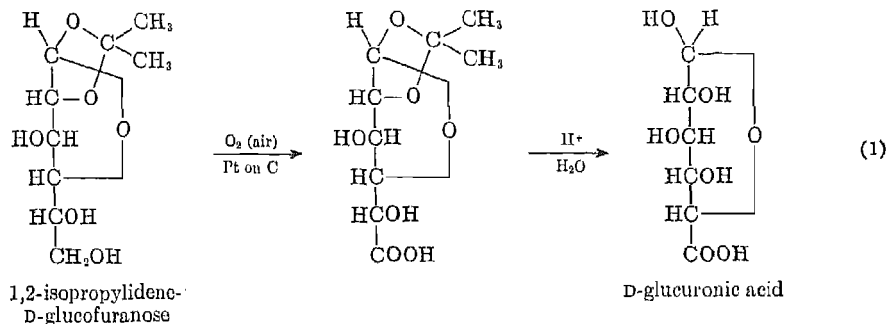
The D-arabinose can be used as such or after oxidation to D-arabonic acid (see p. 268) in one method of synthesizing riboflavin (*q.v.*).

Heating D-gluconic acid under reduced pressure drives off one molecule of water, producing D-glucono-δ-lactone, C<sub>6</sub>H<sub>8</sub>O<sub>6</sub>, formula weight 178.14, long prisms, m.p. 146, [α]<sub>D</sub><sup>20</sup> + 67.5° → + 17.7° (H<sub>2</sub>O, c = 14), soluble in water.

D-Gluconic acid in aqueous solution comes to an equilibrium with D-glucono- $\delta$ -lactone and D-glucono- $\gamma$ -lactone. When such a solution is slowly evaporated under reduced pressure, the  $\delta$ -lactone crystallizes. This lactone has been suggested as the acidulant in baking powders.

**D-Glucuronic acid**,  $C_6H_{10}O_7$ , formula weight 194.14, crystallizes from water in the  $\beta$ -configuration, m.p.  $154\text{--}56^\circ\text{C}$ .,  $[\alpha]_D^{24} + 11.7 \rightarrow 36.3^\circ$  ( $H_2O$ ); it is soluble in water. There are several natural polysaccharides which contain D-glucuronic acid (a hexuronic acid), such as gum arabic, heparin, and hyaluronic acid, although these are not employed as sources.

D-Glucose is the common source and several methods have been announced for the conversion (5). One procedure (13) employs the isopropylidene derivative to protect the carbonyl group. The primary hydroxyl is then oxidized with air in the presence of a platinum-carbon catalyst (eq. 1). Alternative methods employ the methyl glucoside (eq. 2). Oxidants have included permanganate, said to give a 50–60% yield (16), nitrogen dioxide, about 30% yield (15), and nitric acid, 27–33% yield (8). D-Glucuronic acid is recovered from the lactone by acid hydrolysis and crystallization from water. Methyl  $\alpha$ -D-glucoside can be oxidized with oxygen and platinum black in the presence of sodium bicarbonate to the sodium salt of methyl  $\alpha$ -D-glucuronic acid in 87% yield (1). Methyl  $\alpha$ -D-glucoside is sold commercially in 100-lb. bags.



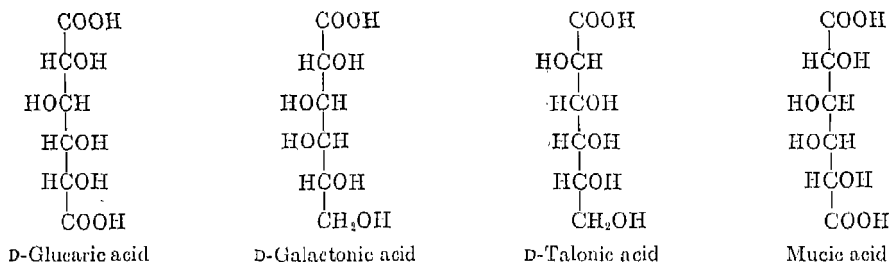
Mammals resort to D-glucuronic acid in the detoxication of phenols and other aromatic compounds. The glucuronides are excreted via the kidneys. Early investigators prepared D-glucuronic acid from the urine of dogs fed borneol or aromatic compounds.

The sodium, potassium, and calcium salts of D-glucuronic acid have been suggested for use as sequestering agents. They are available in limited quantities. A *poly-anhydro-D-glucuronic acid* (oxidized cellulose, U.S.P. XIV (cellulosic acid, N.N.R.))

obtained by oxidation of cellulose with nitrogen dioxide is an effective hemostatic (*q.v.*). D-Glucuronic acid, when heated, loses a molecule of water, producing **D-glucurono- $\gamma$ -lactone**,  $C_6H_8O_6$ , formula weight 176.11, m.p. 175–78°C.,  $[\alpha]_D^{20} +19.2^\circ$  ( $H_2O$ ). It is soluble in water and slowly hydrolyzes to form an equilibrium with the acid. The lactone is available in limited quantities. It has been reported to have some growth-promoting properties, to some extent satisfying the requirements for pantothenic acid (*q.v.*).

**D-Glucaric Acid** (saccharic acid). Oxidation of D-glucose with nitric acid produces D-glucaric acid, tartaric acid, (*q.v.*), oxalic acid (*q.v.*), and carbonic acid. Under controlled conditions, nitrogen tetroxide in chloroform will give a 40% conversion of D-glucose to D-glucaric acid. The acid has been used to a limited extent as a sequestrant. The monopotassium salt has been proposed as a substitute for tartrate in baking powder.

**D-Galactonic Acid and D-Talonic Acid.** D-Galactose can be oxidized with alkaline cupric hydroxide to form D-galactonic and D-talonic acids. Neither has any commercial use.



**D-Galacturonic Acid.** The widespread occurrence of pectins (see *Pectic substances*) in plants makes D-galacturonic acid a common sugar derivative (see Table I). Sugar beet pulp and citrus waste have been proposed as sources for D-galacturonic acid if commercial demand develops. It is present to the extent of 22% in gum arabic and has been recovered from the sulfite liquors from pulping of white pine.

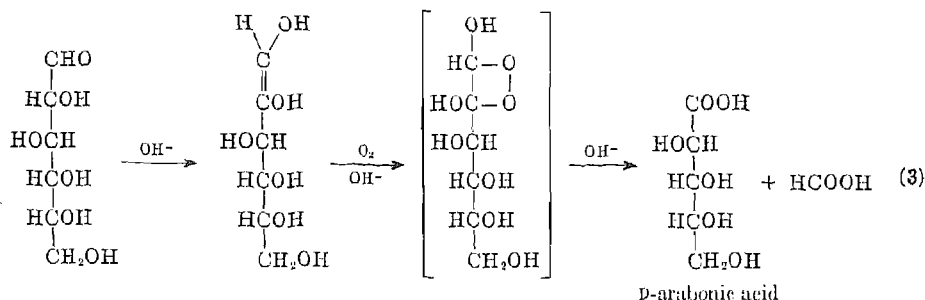
The chief use for D-galacturonic acid is as pectin (the polyuronide). Among proposed uses is a method for a synthesis of L-ascorbic acid starting with D-galacturonic acid (see Vol. 2, p. 157). D-Galacturonic acid has been coupled with isonicotinoyl hydrazide to produce a tuberculostat (*q.v.*).

**Mucic acid** (galactaric acid),  $C_6H_{10}O_8$ , formula weight 210.14, fine white crystals, m.p. 206° (dec.), is soluble in water to the extent of 0.33 g./100 ml. at 14°C., very slightly soluble in ether, and insoluble in ethyl alcohol.

Controlled oxidation of D-galactose with nitric acid produces mucic acid. This reaction is the basis of a traditional method for the estimation of galactose. Mucic acid has been proposed as a substitute for cream of tartar or citric acid in baking powder and in candy.

**D-Arabinic acid**,  $C_6H_{10}O_6$ , formula weight 166.13, m.p. 89°C., is very soluble in water. It can be obtained in 70% yield by air oxidation of D-glucose or D-fructose in alkaline solution (eq. 3). Nitrobenzene or methylene blue exerts a positive catalysis upon the reaction. Invert sugar is a common starting material, and molasses is also a possibility. A limited market for D-arabinic acid has developed as an intermediate (through epimerization to D-ribonic acid) in preparing the ribitol portion of synthetic riboflavin (see Vol. 11, p. 752). Mild heating converts the acid into **D-arabo- $\delta$ -lactone**,

$C_5H_8O_5$ , formula weight 148.11, m.p. 96–98°C.,  $[\alpha]_D^{20} + 73.3^\circ$  ( $H_2O$ ,  $c = 5.8$ ), soluble in water, ethyl acetate, and ethyl alcohol.



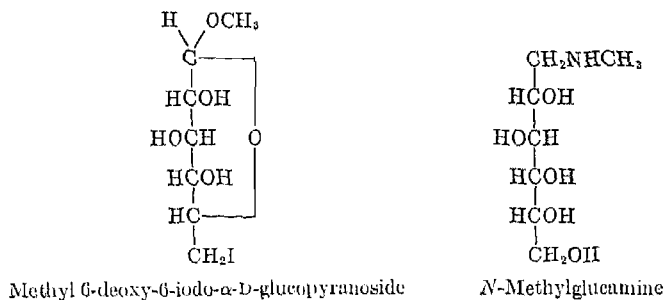
**Lactobionic acid** and **maltobionic acid** are examples of aldonic acids that may be obtained from reducing disaccharides, such as lactose and maltose, by means of fermentation and chemical oxidation.

#### MISCELLANEOUS DERIVATIVES

Sugar derivatives such as **sucrose ethers**, because of their polyfunctional nature, have received considerable study as components of plastic materials but none of these suggestions has been put to practical use. Benzyl, ethyl, allyl, and crotyl ethers of sucrose are said to plasticize cellulose ester polymers. The allyl ethers of sucrose appear to be useful as a coating resin with somewhat superior resistance to organic solvents. Allyl sucrose also has received some attention for upgrading semidrying oils. Ethylidene sucrose will give vinyl-type polymers when catalyzed with boron trifluoride.

**Other sugar derivatives** have a wide diversity of applications but none is of any considerable commercial significance. For example, oral ingestion of *methyl 6-deoxy-6-iodo- $\alpha$ -D-glucopyranoside* or the corresponding galactose derivative causes kidney structures to become opaque to x-rays.

If glucose in liquid ammonia is hydrogenated in the presence of Rancy nickel at 50–100 atm. pressure and 75–125°C., *glucamine* (D-glucitylamine) is formed. When methylated on the nitrogen, the product is *N-methylglucamine*. A variety of applications of this product have been suggested. For example, it is said to facilitate bright-plating with cadmium. With formaldehyde, phenol, and fluosilicic acid, it produces a water-soluble mothproofing substance. With chloroethanesulfonic acid and methylamine, a product is formed which will couple with aromatic diazonium salts to yield dyes. Condensed with cetyl chloride, glucamine yields a detergent.



The stearic hydrazide derivatives of sugars are said to impart a "soft handle" to cotton cloth. A urea-glucose condensation product is said to induce crease resistance. Cupric sucate and a condensate of a sugar oxime with acrylonitrile have been said to be insecticides.

### Bibliography

- (1) Barker, S. A., Bourne, E. J., and Stacey, M., *Chemistry & Industry*, **1951**, 970.
- (2) Blom, R. H., Pfeifer, V. F., Moyer, A. J., Trauffer, D. H., Conway, N. F., Crocker, C. K., Farison, R. E., and Hannibal, D. V., *Ind. Eng. Chem.*, **44**, 435 (1952).
- (3) Dickey, F. E., and Wolfrom, M. L., *J. Am. Chem. Soc.*, **71**, 825 (1949).
- (4) Gould, B. S., *Chemical Compounds Formed from Sugar by Molds*, Sugar Research Foundation, N.Y., 1947.
- (4a) Isbell, H. S., and Frish, H. L., *J. Research Natl. Bur. Standards*, **6**, 1145 (1931).
- (5) Mehlretter, C. L., in Hudson, C. S., and Wolfrom, M. L. (eds.), *Advances in Carbohydrate Chemistry*, Vol. VIII, Academic Press, N.Y., 1953, pp. 231-50.
- (6) Morton, A. A., *Levulinic Acid as a Source of Heterocyclic Compounds*, Sugar Research Foundation, N.Y., 1947.
- (7) Prescott, F. J., Shaw, J. K., Bilello, J. P., and Cragwell, G. O., *Ind. Eng. Chem.*, **45**, 338 (1953).
- (8) Brit. Pat. 670,929 (Apr. 30, 1952), Corn Products Refining Co.
- (9) U.S. Pat. 2,052,029 (Aug. 25, 1936), B. R. Harris.
- (10) U.S. Pat. 2,060,850 (Nov. 17, 1936), W. S. Calcott and R. G. Clarkson (to Du Pont).
- (11) U.S. Pat. 2,091,105 (Aug. 24, 1937), H. A. Piggott (to Imperial Chemical Industries).
- (12) U.S. Pat. 2,212,521 (Aug. 27, 1940), B. R. Harris (to Colgate-Palmolive-Peet Co.).
- (13) U.S. Pat. 2,562,200 (July 31, 1951), C. L. Mehlretter (to U.S.A.).
- (14) U.S. Pat. 2,584,017 (Jan. 29, 1952), J. Dvorkovitz and T. G. Hanley, Jr. (to Diversey Corp.).
- (15) U.S. Pat. 2,592,249 (Apr. 8, 1952), D. H. Couch and E. A. Cleveland (to Corn Products Refining Co.).
- (16) U.S. Pat. 2,592,266 (Apr. 8, 1952), D. M. Gallagher (to Corn Products Refining Co.).

### GENERAL REFERENCES

- (17) Bates, F. J., et al., "Polarimetry, Saccharimetry and the Sugars," *Natl. Bur. Standards (U.S.), Circ.*, **C440** (1942).
- (18) Bode, H. E., *Sugar Derivatives: A Survey of Potential Production Costs*, Sugar Research Foundation, N.Y., 1949.
- (19) Degering, E. F., *Chemistry of the Carbohydrates*, John S. Swift Co., Cincinnati, Ohio, 1943.
- (20) Evans, T. H., and Hibbert, H., *Bacterial Polysaccharides*, Sugar Research Foundation, N.Y., 1947; *Advances in Carbohydrate Chemistry*, **2**, 203 (1946).
- (21) Guttag, A., *Patents on the Reactions of Sugars*, Sugar Research Foundation, N.Y., 1947.
- (22) Long, L., *Sugar and Sugar By-Products in the Plastics Industry*, Sugar Research Foundation, N.Y., 1949.
- (23) Pigman, W. W., and Goeppe, R. M., Jr., *Chemistry of the Carbohydrates*, Academic Press, N.Y., 1948.
- (24) Pittenger, P. S., *Sugars and Sugar Derivatives in Pharmacy*, Sugar Research Foundation, N.Y., 1947.
- (25) Underkoffler, L. A., and Hickey, R. J., *Industrial Fermentations*, Chemical Pub. Co., N.Y., 1954, Vol. I.
- (26) Whistler, R. L., and Smart, C. L., *Polysaccharide Chemistry*, Academic Press, N.Y., 1953.

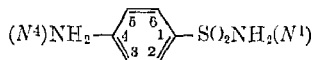
J. L. HICKSON

**SUINT.** See *Textile technology*; *Wool*.

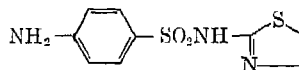
**SULFA-.** For many names beginning with sulfa-, see *Sulfa drugs*.

## SULFA DRUGS

Sulfa drugs are sulfonamides (*q.v.*), most of which are derived from sulfanilamide (*p*-aminobenzenesulfonamide) (I), the chemotherapeutically active derivatives being in most cases those substituted in the *N*<sup>1</sup>-position, such as sulfathiazole (II). *p*-Nitrosulfathiazole, *p*-2,4-diaminophenylazobenzenesulfonamide hydrochloride (2,4-diamino-4'-sulfamoylazobenzene hydrochloride, Prontosil), and *p*-(aminomethyl)-benzenesulfonamide (Sulfamylon), closely related in structure and activity, are also included.



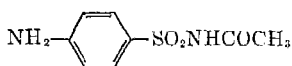
(I) Sulfanilamide



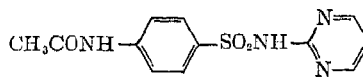
(II) Sulfathiazole

The sulfa drugs are antibacterial agents, bacteriostatic rather than germicidal in action, which are used alone or in various combinations with each other or with antibiotics (15,26,27) in the treatment of many types of infection such as those caused by  $\beta$ -hemolytic streptococci or pneumococci. See also *Antiseptics*.

The principal chemical classes of sulfa drugs are the *N*<sup>1</sup>-heterocyclic derivatives (typified by sulfathiazole (II)), the *N*<sup>1</sup>-acyl derivatives (as sulfacetamide (III)), and the *N*<sup>1</sup>-derivatives (as acetylsulfadiazine (IV) (an intermediate in the preparation of sulfadiazine), which is also an *N*<sup>1</sup>-heterocyclic derivative). The common or generic names are most used, but systematic names can be derived with sulfanilamide (or a carboxamide in the case of RCO-acyl derivatives) as the parent compound. See Table I.



(III) Sulfacetamide



(IV) Acetylsulfadiazine

For a review having a complete tabulation of over 5000 sulfanilamide derivatives, along with descriptions of preparation and properties, trade and other names, and much information covering the literature through 1944, see Northey (27).

**History.** In a sense the sulfa drugs were an outgrowth of Ehrlich's idea of the mechanism of action of chemotherapeutic agents. The early efforts of Morganroth and Levey with modified antimalarial alkaloids of the cinchona group and of Heidelberger and Jacobs (27, p. 1, ref. 188) with the coupling product of dihydrocupreine with diazotized sulfanilamide were unsuccessful. These were followed by Mietzsch's and Klarer's (27, p. 1, ref. 357; 45) synthesis and Domagk's (27, p. 2, ref. 987) testing of Prontosil. An important factor in this discovery was the use of an *in vivo* test in mice, since an *in vitro* test of Prontosil would have shown no activity.

The studies of the French workers Tréfouël, Tréfouël, Nitti, and Bovet (27, p. 3, ref. 511), and others (27, p. 3, ref. 170) led to the important fundamental discovery that the sulfanilamide component was the active part of the sulfanilamide azo dyes. Confirmation of this by the British workers Colebrook (27, p. 4, ref. 897) and Buttle and their co-workers (27, p. 4, ref. 61) stimulated research programs in synthesis and testing of sulfanilamide derivatives throughout the world.

This intensive research led to the synthesis of much more effective *N*<sup>1</sup>-heterocyclic-substituted sulfanilamides, and added the complication that, since most of the

TABLE I. Common Sulfu Drugs.

Generic name	Chemical name	Empirical formula	Status	M.p., °C.	Solubility in water, ml. to dissolve 1 g. at 25° C.	References
Sulfanilamide (I)	Sulfanilamide	$C_6H_5N_2O_2S$	U.S.P. XIV	164.5-166.5	125	36
Sulfapyridine (V)	N <sup>1</sup> -2-Pyridylsulfanilamide	$C_{11}H_{11}N_3O_2S$	N.F. IX	191-193	3,500	25, 47
Sodium sulfapyridine	—	$C_{11}H_{10}N_3NaO_2S \cdot H_2O$	N.F. IX	—	1.5	25
Sulfadiazine (VI)	N <sup>1</sup> -2-Pyrimidinylsulfanilamide	$C_{10}H_{10}N_4O_2S$	U.S.P. XIV, N.N.R.	252-256	13,000	36, 57, 58
Sodium sulfadiazine	—	$C_{10}H_9N_4NaO_2S$	U.S.P. XIV, N.N.R.	—	2	36
Sulfamerazine	N <sup>1</sup> -(4-Methyl-2-pyrimidinyl)-sulfanilamide	$C_{11}H_{12}N_4O_2S$	U.S.P. XIV, N.N.R.	234-238	6,250	36, 57
Sodium sulfamerazine	—	$C_{11}H_{11}N_4NaO_2S$	U.S.P. XIV	—	3	36
Sulfamethazine	N <sup>1</sup> -(4,6-Dimethyl-2-pyrimidinyl)sulfanilamide	$C_{12}H_{14}N_4O_2S$	N.N.R.	197-200	—	26, 57
Sulfadimetine <sup>a</sup> (VII)	N <sup>1</sup> -(2,6-Dimethyl-4-pyrimidinyl)sulfanilamide	$C_{12}H_{14}N_4O_2S$	—	233-243	—	53
Sulfapyrazine (VIII)	N <sup>1</sup> -2-Pyrazinylsulfanilamide	$C_{10}H_{10}N_4O_2S$	N.N.R., 1947	251, 255-257 dec.	—	62
Sulfaguinoxaline (IX)	N <sup>1</sup> -2-Quinoxalinyisulfanilamide	$C_{14}H_{12}N_4O_2S$	—	249.5-250	—	37, 56
Sulfisoxazole <sup>b</sup> (X)	N <sup>1</sup> -(3,4-Dimethyl-5-isoxazolinyisulfanilamide	$C_{11}H_{13}N_3O_2S$	N.N.R.	193	—	26, 65
Sulfathiazole (II)	N <sup>1</sup> -2-Thiazolylsulfanilamide	$C_9H_9N_3O_2S_2$	U.S.P. XIV	200-204	1,700	36, 54
Sodium sulfathiazole	—	$C_9H_8N_3NaO_2S_2 \cdot 1\frac{1}{2}H_2O$	U.S.P. XIV	—	2.5	36
Sulfacetamide <sup>c</sup> (III)	N-Sulfanilylacetamide	$C_8H_{10}N_2O_3S$	N.N.R.	181-184	140	26, 59



Sodium sulfacetamide	---	$C_8H_9N_3NaO_5S.H_2O$	N.N.R.	---	2.5	26
Sulfabenzamide	N'-Sulfamylbenzamide	$C_{13}H_{12}N_2O_3S$	---	181.2-182.3	---	63
Sulfaguanidine (XIII)	N'-Guanylsulfanilamide, N'-amidinosulfanilamide	$C_7H_9N_5O_5S.H_2O$	U.S.P. XIV	190-193	1,000	36, 46
Succinylsulfathiazole <sup>d</sup> (XIV)	4'-(2-Thiazolylsulfamoyl)-succinamic acid	$C_{13}H_{13}N_3O_5S_2.H_2O$	U.S.P. XIV, N.N.R.	---	4,800	36, 49, 50
Phthalylsulfathiazole <sup>e</sup>	4'-(2-Thiazolylsulfamoyl)-phthalanilic acid	$C_{17}H_{13}N_3O_5S_2$	U.S.P. XIV, N.N.R.	darkens 244-250, melts 272-277, (preheat bath 220)	---	36, 49, 51
p-Nitrosulfathiazole <sup>f</sup>	N-(2-Thiazolyl) p-nitrobenzenesulfonamide	$C_9H_7N_3O_4S_2$	N.N.R.	255-262	---	26, 54
Prontosil <sup>g</sup> (XV)	p-(2,4-Diaminophenylazo)-benzenesulfonamide hydrochloride	$C_{12}H_{12}N_4O_3S.HCl$	---	247-251	---	35, 45
Sulfamylon <sup>h</sup> (XVI)	p-(Aminomethyl)benzenesulfonamide, $\alpha$ -aminotoluenesulfonamide, 4-homosulfanilamide	$C_7H_9N_3O_3S$	---	153	---	35, 48

<sup>a</sup> Brand name, Elkosin.<sup>b</sup> Brand name, Gantrisin.<sup>c</sup> Brand name, Sulamyl.<sup>d</sup> Brand name, Sulfasuxidine.<sup>e</sup> Brand name, Sulfathalidine.<sup>f</sup> Brand name, Nisulfazole.<sup>g</sup> Brand name.

TABLE II. Optical Crystallographic Properties of Sulfonamides.

Compound	Habit	System	Extinction	Elongation	2V	Optical sign	Dispersion	Refractive indexes at 25°			References
								Alpha	Beta	Gamma	
Sulfanilamide monohydrate:											
A	—	Ortho- rhombic	—	±	—	+	None	1.505	1.639	> 1.85	67
B	—	Mono- clinic	—	—	—	+	$v > r$	1.555	1.672	> 1.85	67
C	—	Mono- clinic	—	+	—	+	None	1.547	1.633	> 1.85	67
Sulfanilamide											
Sulfapyridine (stable form)	—	—	—	—	—	—	—	1.570	1.677	> 1.733	33
Sulfapyridine Phase I	—	—	—	—	—	—	—	1.680	1.733	> 1.733	33
Sulfapyridine Phase II	Tabular to equant	Mono- clinic	$Y \parallel b$ , $Z \wedge c = 39^\circ$	±	88°	+	V. strong, axial, $r > v$	1.670	1.736	1.813	12
Sulfapyridine Phase III	Lath shaped	Mono- clinic	$Y \parallel b$ , $X \wedge c = 38^\circ$	Parallel to $b$ , ±	36	—	Inclined, $v > r$	1.585	1.722	1.739	12
Sulfapyridine Phase III	Lamellar	(Ortho- rhombic	$X = a$ , $Y = b$ , $Z = a$	±	Very large	+	Strong rhombic, $v > r$	Indeter- minable	1.697	1.721	12
Sulfapyridine Phase IV	Tabular	Mono- clinic	$Y \parallel b$ , $Z \wedge c = 44^\circ$	Parallel to $b$ , ±	74°	+	Axial, $r > v$	1.625	1.693	1.835	12
Sulfapyridine Phase V	Equant	Triclinic?	?	?	Very small	—	Strong, $r > v$	Indeter- minable	1.745	1.761	12
Sulfadiazine	—	Mono-	$Y \parallel b$ , $Z \wedge c = 20^\circ$ (?)	Parallel to $b$	45–46°	+	—	1.680	1.697	1.788	68

Sulfadiazine	—	—	—	—	—	—	—	1.615	1.663	1.734	33
Sulfadiazine	Lath shaped	Mono- clinic	$Y \parallel b$ , $Z \wedge c = 35^\circ$	Parallel to $b$ , $\pm$	76°	+	Axial, $r > v$	1.596	1.675	1.830	13
Sulfamerazine	Tabular	(Ortho- rhombic	Parallel	$\pm$	58	—	$V$ , strong rhombic, $r > v$	1.568	1.657	1.687	13
Sulfamerazine	—	—	—	—	—	—	—	1.587	—	1.675	33
Sulfathiazole	—	—	—	—	—	—	—	1.674	1.685	> 1.733	33
Sulfathiazole I	Hexagonal prisms and plates	—	—	—	Small	+	—	1.674	1.733	> 1.733	27
Sulfathiazole II	Prismatic rods	—	Parallel	—	—	—	—	1.605	1.733	> 1.733	27
Sulfathiazole II	Lath shaped	Mono- clinic	$Y \parallel b$ , $X \wedge c = 23^\circ$	Parallel to $b$ ( $\pm$ )	52°	—	Inclined, $r > v$	1.598	1.741	1.780	13
Sulfacetamide	Columnar	Ortho- rhombic	Symmetrical	Parallel to $c$	21°	+	None	1.559	1.564	1.727	13
Sulfaguanidine (monohydrate)	Lath shaped	Mono- clinic	$Y \parallel b$ , $Z \wedge c = 17^\circ$	Parallel to $b$ ( $\pm$ )	86°?	+	Axial, $r > v$	1.586	1.649	1.731	13
Sulfaguanidine	—	—	—	—	—	—	—	1.606	1.663	1.734	33
Succinylsulfathiazole I	—	Mono- clinic	—	—	—	—	Strong, $v > r$	1.578	1.676	1.710	40
Succinylsulfathiazole II	—	Triclinic	—	—	—	—	None	1.54	1.61	1.73	40

active compounds were prepared independently by several groups, many patent interferences resulted.

### Physical and Chemical Properties

The sulfa drugs are white or nearly white powders melting above 150°C. The solubilities of the sulfa drugs and their acetyl derivatives have been widely studied (3; 19; 27, p. 458, ref. 1173, p. 494, ref. 1122; 30; 33) particularly in body fluids or buffered solutions, in order to better understand the behavior of these materials in the body. These compounds are usually not very soluble in cold water, and are somewhat more soluble in acetone. Sulfanilamide, sulfaguanidine, sulfacetamide, and *p*-(aminomethyl)benzenesulfonamide are fairly soluble in hot water. See Table I.

The optical crystallographic properties of most of the official sulfa drugs have been determined. (See Table II.)

Bell and Roblin (2) have determined  $pK_a$  values for a number of the *N*<sup>1</sup>-substituted sulfanilamide derivatives. See also p. 281.

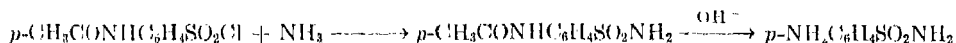
With the exception of sulfaguanidine, the sulfa drugs in common use are soluble in strong aqueous alkali. The *N*<sup>1</sup>-acyl derivatives, sulfacetamide and sulfabenzamide, are soluble in sodium bicarbonate, as are succinylsulfathiazole and phthalylsulfathiazole. The sodium salts of the *N*<sup>1</sup>-heterocyclic-substituted sulfa drugs are very soluble in water, giving alkaline solutions. The sulfonamide linkage is in general quite stable to aqueous alkali, although sulfacetamide and sulfaguanidine may be hydrolyzed with this reagent.

The sulfa drugs having a free 4-amino group are rather soluble in aqueous strong mineral acids such as hydrochloric or sulfuric acid. Heating with strong aqueous acid cleaves the sulfonamide linkage in some cases (27, p. 14, ref. 102).

The 4-amino group is readily diazotized with nitrous acid, and is the basis for several types of assay (see p. 282). Acylation on the 4-amino group takes place readily with agents such as acetic anhydride or phthalic anhydride. Aldehydes react readily with the 4-amino group to form anils and other condensation products (7,9; 27, p. 45). Sugar derivatives and various aldehyde bisulfite combinations (27, p. 47) have been prepared for purposes of solubilization, but the effectiveness of these compounds is due to their degradation in the body to the parent sulfanilamide compound. Bromine reacts readily with the sulfanilamide derivatives, substituting on the benzene ring (27).

### Preparation and Manufacture

**Sulfanilamide (I).** *N*-Acetylsulfanilyl chloride (ASC) (from the chlorosulfonation of acetanilide, see Vol. 1, p. 52), the basic raw material for most of the sulfonamide drugs, is treated with concentrated aqueous ammonia, and the *N*<sup>1</sup>-acetyl group is removed by alkali (18; 27, p. 14):



Certain other *N*-acylsulfanilyl chlorides, such as those prepared from formanilide, oxanilide, or carbanilide, may be used in place of ASC (27, p. 13). The economics of these processes probably would depend on the availability and price of the different acyl derivatives. In Germany, carbethoxyaminobenzenesulfonyl chloride (*N*-ethoxycarbonylsulfanilyl chloride), *p*-C<sub>2</sub>H<sub>5</sub>OOCNHC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>Cl, was often used, partly because of less difficulty in drying than with ASC (18).

Chlorobenzene may be chlorosulfonated and then treated with strong aqueous ammonia in an autoclave at 160° using a copper catalyst to obtain sulfanilamide (27, p. 13).

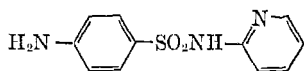
#### N<sup>1</sup>-HETEROCYCLIC DERIVATIVES

**Sulfapyridine** (V), reported in 1938 by Whitby (27, p. 4, ref. 549), was the first of this highly effective series to be prepared (27, p. 4, ref. 171, p. 14, ref. 102, p. 68, ref. 553; 47). The most effective method of preparing this compound is the reaction between dry ASC and 2-aminopyridine in dry pyridine (27, p. 14, p. 68, refs. 434, 435; 40; 47). The acetylsulfapyridine may be recovered by one of the following methods. (1) Water and alkali are added to the reaction mixture, the pyridine is distilled off, and the residue is acidified with sulfur dioxide, precipitating the compound from solution. (2) The reaction mixture is first diluted and acidified, *N*<sup>1</sup>-acetylsulfapyridine precipitates from solution and is filtered off. The acetyl group is removed by hydrolysis with aqueous alkali, and sulfapyridine is precipitated with acid. Purification is carried out either by a recrystallization from alcohol or acetone, using activated charcoal for decolorization, or by dissolving the compound in water and alkali, treating with activated charcoal, clarifying and precipitating with acid (27, p. 14).

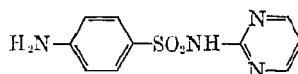
An alternate preparation is the action of ASC on 2-aminopyridine in water in the presence of an alkali, 18; 27, p. 14), followed by hydrolysis and acidification.

Several other processes have been developed, mostly for patent purposes, where other acid chlorides are used in place of ASC with 2-aminopyridine in pyridine (27, p. 15): *p*-nitrobenzenesulfonyl chloride or azobenzenesulfonyl chloride (1), followed by reduction (27, p. 7, ref. 341); *p*-nitrobenzenesulfonyl chloride, NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>SOCl, followed by oxidation of the sulfenamide to the sulfonamide and reduction of the nitro group (67); sulfanilyl fluoride (27, p. 14); acetamidobenzenesulfonyl chloride, with oxidation to the sulfonamide and deacetylation (67,70); and phthalimidobenzenesulfonyl chloride, followed by cleavage with hydrazine (60).

Methods avoiding the use of pyridine involve: reaction of ASC with the sodium salt of 2-aminopyridine in an inert solvent; heating 2-bromo- or 2-iodopyridine with sulfanilamide, potassium carbonate, and copper powder (27, p. 14, ref. 341); reaction of ASC and 2-aminopyridine using an excess of the latter as hydrogen chloride acceptor (27, p. 13).



(V) Sulfapyridine



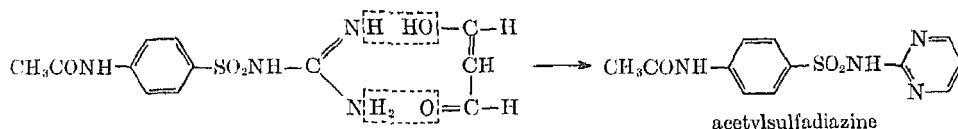
(VI) Sulfadiazine

**Sulfadiazine** (VI), first synthesized by Roblin, Williams, Winnek and English (27, p. 4, ref. 434), is prepared by the reaction between ASC and 2-aminopyrimidine in pyridine (27, p. 4, ref. 434, p. 13, p. 18, ref. 493; 57; 58; 64). Other acid chlorides than ASC also are used as in the case of sulfapyridine (18,27).

*N*<sup>1</sup>-Pyrimidinylsulfanilamides substituted in the pyrimidine ring may be prepared by reactions between sulfanilamide and 2-chloropyrimidines, 2-alkylmercaptopyrimidines, or 2-nitraminopyrimidines.

A ring closure type of reaction is also used to prepare sulfadiazine: Sulfaguanidine (see p. 279), *N*<sup>1</sup>-acetylsulfaguanidine (or *p*-nitrobenzenesulfonylguanidine) is cou-

densed with malonaldehyde or one of its derivatives, such as 1,1,3,3-tetraethoxypropane or ethoxyacrolein acetal, followed by alkaline hydrolysis (or reduction):



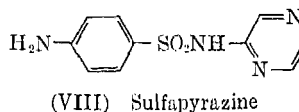
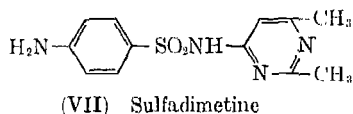
Propionaldehyde (propargylaldehyde) or its acetals may be used in place of malonaldehyde (44,75).

As a general process for preparing these compounds, the various para-substituted benzenesulfonylguanidines are treated with the appropriate 1,3-diketo compounds (66,77).

**Sulfamerazine** is prepared by methods similar to those described for sulfadiazine (18; 27, p. 4, ref. 434, p. 18, ref. 493; 57). Other reactions involve the use of the intermediate  $\text{CH}_3\text{COCH}=\text{CHCl}$  (74),  $\text{CH}_3\text{COCH}_2\text{CH}(\text{OCH}_3)_2$  (27, p. 1, ref. 188), or  $\text{CH}_3\text{C}(\text{OC}_2\text{H}_5)=\text{CHCH}(\text{OC}_2\text{H}_5)_2$  (43) with sulfaguanidine or *N*<sup>4</sup>-acetylsulfaguanidine.

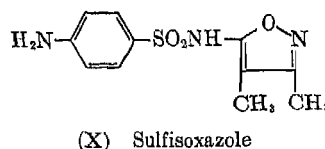
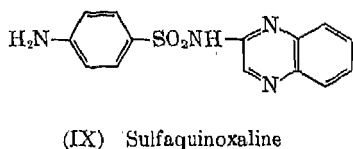
**Sulfamethazine** is prepared by methods described under sulfadiazine (27, p. 13, p. 18, ref. 493, p. 31, ref. 66; 57). Another important method involves the reaction between sulfaguanidine and acetylacetone,  $\text{CH}_3\text{COCH}_2\text{COCH}_3$ .

**Sulfadimetine** (VII) is more difficult to prepare owing to the different character of the 4-amino group from the 2-amino group of this pyrimidine component. The condensation of two moles of ASC per mole of 4-amino-2,6-dimethylpyrimidine, with trimethylamine as hydrogen chloride acceptor, gives the bis(acetylsulfanilyl) derivative, readily hydrolyzable to sulfadimetine (23). Alternatively, the more stable *p*-nitrobenzenesulfonyl chloride (one mole) is sometimes used in place of ASC in the usual reaction (53) as it gives fewer side reactions with pyridine.



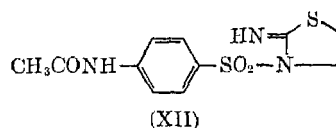
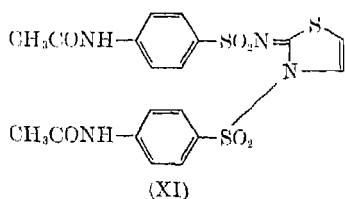
**Sulfapyrazine** (VIII) is prepared by reactions similar to those used for sulfadiazine, involving the usual ASC reaction with 2-aminopyrazine (11; 27, p. 79, ref. 452; 62). Another method is the reaction between sulfanilamide (68) and 2-chloropyrazine.

**Sulfaquinoxaline** (IX) (37,56) and **sulfisoxazole** (X) (59) are prepared by methods similar to those used for sulfadiazine:



**Sulfathiazole** (II), first reported by Fosbinder and Walter (27, p. 4, ref. 149), is prepared by processes similar to those used for sulfapyridine (27, p. 4, refs. 149,434, p. 13, 54).

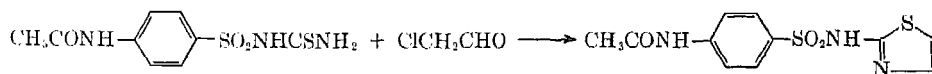
Although the reaction in pyridine is probably the most efficient method, use has been made of the aqueous reaction of ASC and 2-aminothiazole in the presence of alkali, whereby a bis-substituted compound (XI) is obtained (18,55,78):



This may be hydrolyzed directly with sodium hydroxide to sodium sulfathiazole (18), or it may be used as an acylating agent. By heating compound (XI) with ammonia, a mixture of *N*<sup>4</sup>-acetylsulfathiazole and *N*<sup>4</sup>-acetylsulfanilamide is obtained; and heating with guanidine gives a mixture of *N*<sup>4</sup>-acetylsulfathiazole and *N*<sup>4</sup>-acetylsulfaguandine (79). The acetyl group is removed by hydrolysis.

Another preparation is that in which ASC and 2-aminothiazole are condensed with the aid of aqueous sodium bicarbonate to give the ring-nitrogen-substituted compound (XII), which rearranges under the influence of heat to *N*<sup>4</sup>-acetylsulfathiazole (71).

The thiazole component is formed last in the following process (52):



The acetyl group is hydrolyzed by heating in aqueous sodium hydroxide.

Purification procedures are similar to those used for sulfapyridine (27).

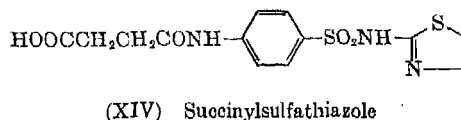
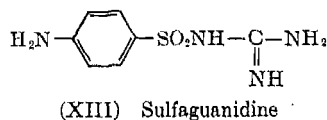
#### *N*<sup>1</sup>-ACYLSULFANILAMIDES

*N*<sup>1</sup>-Acylsulfanilamides, in general, are prepared by types of reactions such as: acylation of an *N*<sup>4</sup>-substituted sulfanilamide in the *N*<sup>1</sup>-position in the presence of strong mineral acid (75) followed by hydrolysis of the *N*<sup>4</sup> group; or reaction between ASC and the sodium salt of an acylamide, followed by hydrolysis of the *N*<sup>4</sup>-acetyl group (61).

**Sulfacetamide** (III), synthesized independently by two groups (27, p. 5, ref. 115, p. 37, ref. 101), is prepared by acetylating *N*<sup>4</sup>-acetylsulfanilamide with acetic anhydride alone, or acetyl chloride in pyridine, followed by hydrolysis of the *N*<sup>1</sup>-acetyl group. Other *N*<sup>4</sup>-acylated benzenesulfonamides may be acetylated on the *N*<sup>1</sup>-nitrogen and the *N*<sup>4</sup>-substituent then converted to an amino group (18,59).

**Sulfabenzamide** is prepared by *N*<sup>1</sup>-acylation of *N*<sup>4</sup>-acetylsulfanilamide in aqueous alkali with benzoyl chloride and hydrolysis of the 4-acetyl group (27, p. 37, ref. 101; 63).

**Sulfaguandine** (XIII) is prepared by the condensation of ASC and guanidine salts in the presence of sodium hydroxide, usually in an organic solvent such as a ketone (27, p. 16, ref. 17; 76) and the *N*<sup>4</sup>-acetyl group is removed by either acid or alkaline hydrolysis.



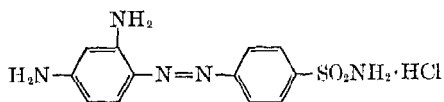
N<sup>1</sup>-HETEROCYCLIC N<sup>4</sup>-ACYLSULFANILAMIDE DERIVATIVES

**Succinylsulfathiazole** (XIV) is prepared either by reaction of succinic anhydride with sulfathiazole, or of succinylsulfanilyl chloride (4'-chlorosulfonylsuccinanilic acid) with 2-aminothiazole (27, p. 16, ref. 372; 49; 50). Similar methods are used for **phthalylsulfathiazole** (27, p. 16, ref. 372; 49; 51).

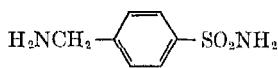
## MISCELLANEOUS COMPOUNDS

**p-Nitrosulfathiazole** can be synthesized by the reaction between *p*-nitrobenzenesulfonyl chloride and 2-aminothiazole in pyridine (54).

**Prontosil** (*p*-(2,4-diaminophenylazo)benzenesulfonamide hydrochloride) (XV), is prepared by diazotizing sulfanilamide and coupling with *m*-phenylenediamine (18,45).



(XV) *p*-(2,4-Diaminophenylazo)benzenesulfonamide hydrochloride



(XVI) *p*-(Aminomethyl)benzenesulfonamide

**p-(Aminomethyl)benzenesulfonamide** (XVI) is synthesized from *N*-benzylacetamide by chlorosulfonating, treating the resulting acetamidomethylbenzenesulfonyl chloride with aqueous ammonia, and hydrolyzing (18; 27, p. 252, ref. 361; 48).

## General Economic Aspects

The production of sulfa drugs increased rapidly, spurred on by military needs, reaching a maximum of over ten million pounds in 1943. The abrupt drop to less than half this amount in 1944 coupled with the commercial development of antibiotic production led to the belief that the sulfa drugs would be replaced rapidly, or at least reduced to a very low level. However, production has been maintained at somewhat over the 1944 level in spite of the very rapid increase in production of antibiotics. The greatly increased veterinary use as well as their low cost and effectiveness in therapy has helped to maintain the market. The U.S. production of sulfa drugs based on U.S. Tariff Commission figures is shown in Table III.

## Mechanism of Action

The mechanism of action of the sulfa drugs has been the subject of intensive studies from the time of the discovery of their usefulness (5,15,27,29,40,41,42).

Woods' (40) discovery that *p*-aminobenzoic acid (see Vol. 2, p. 473) is a potent inhibitor of the sulfa drugs and the evolution by Woods and Fildes (12) of the theory which correlated the antagonism between sulfa drugs and *p*-aminobenzoic acid were important in the understanding of this mechanism of action. The theory postulates that *p*-aminobenzoic acid is an essential metabolite for the bacteria involved, and the primary action of the sulfa drugs is a competitive inhibition of one or more enzyme reactions in which *p*-aminobenzoic acid is concerned. There is considerable evidence that at least one of the functions of *p*-aminobenzoic acid is in the synthesis of folic acid and possibly in the synthesis of nucleic acids and certain amino acids.

Bell and Roblin (2), making use of the Woods-Fildes theory and molecular structure consideration, were able to correlate *in vitro* activity and structure of new sul-



TABLE III. Production of Sulfa Drugs in the United States.

	Sulfa drugs, lb. × 1000			Antibiotics, lb. × 1000		
	Total	Sulfanilamide	Sulfathiazole	Total	Penicillin salts	Streptomycin and dihydrostreptomycin
1937	—	355	—	—	—	—
1938	—	339	—	—	—	—
1939	—	709	—	—	—	—
1940	"	543	92 <sup>b</sup>	—	—	—
1941	2,091	995	561	—	—	—
1942	5,435	2146	1,594	—	—	—
1943	10,006	2953	—	—	—	—
1944	4,515	748	1,499	2.6 <sup>c</sup>	2.6 <sup>d</sup>	—
1945	5,888	—	2,086	12.3 <sup>c</sup>	12.3 <sup>d</sup>	—
1946	5,104	—	2,016	48 <sup>e</sup>	45 <sup>d</sup>	2.6
1947	6,142	—	2,698	93 <sup>e</sup>	70 <sup>d</sup>	22.6
1948	2,660	<sup>f</sup>	866	243 <sup>e</sup>	162	82
1949	4,895	—	1,566	443 <sup>e</sup>	249	193
1950	4,967	—	1,064	852 <sup>g</sup>	429	203
1951	6,411	—	1,456	1,286 <sup>h</sup>	625	354
1952	5,786	—	724	1,487 <sup>h</sup>	671	387
1953	4,672	—	—	1,630 <sup>h</sup>	753	430

<sup>a</sup> 102,000 lb. sulfapyridine produced; no other sulfapyridine figures are given.

<sup>b</sup> Sales of sulfathiazole. No production figure given for sulfathiazole in 1940.

<sup>c</sup> Penicillin only.

<sup>d</sup> Calculated from Oxford units listed, at the rate of 604 million Oxford units per lb. in 1947.

<sup>e</sup> Penicillin plus streptomycins.

<sup>f</sup> 35,000 lb. sulfacetamide produced in 1948; no other figures given for this compound.

<sup>g</sup> Except animal feed.

<sup>h</sup> For human and veterinary use.

In 1937, there was sold 267,000 lb. sulfanilamide valued at \$1,322,000 at \$4.95 a lb.

In 1946, there was sold 5,147,000 lb. of all sulfa drugs for \$23,357,000 (\$4.51 per lb.); and 20,363 lb. antibiotics for \$95,671,000 (almost \$4,700 per lb.).

In 1952, 3,092,000 lb. sulfa drugs for \$15,910,000 (\$5.15 per lb.); and 1,321,000 lb. antibiotics for \$266,574,000 (\$202 per lb.).

fanilamide derivatives. From studies of acid dissociation constants and *in vitro* bacteriostatic activities, it was observed that maximum activity of *N*<sup>1</sup>-substituted sulfanilamides occurs when the *pK<sub>a</sub>* of the derivative is 6.7. The theory is stated as follows: The more negative the SO<sub>2</sub> group of an *N*<sup>1</sup>-substituted sulfanilamide derivative, the greater the bacteriostatic activity of the compound. However, certain anomalies are difficult to explain on the basis of this or other theories.

#### RELATION BETWEEN STRUCTURE AND CHEMOTHERAPEUTIC ACTIVITY

Since clinical effectiveness depends upon absorption, excretion, metabolism, and inherent activity, it is difficult to relate structure and activity in treatment of diseases. For sulfa drugs, chemotherapeutic activity is interpreted as activity against susceptible strains of  $\beta$ -hemolytic streptococci *in vitro* or *in vivo* that is antagonized by *p*-aminobenzoic acid. The following generalizations have been made (27, p. 422).

Nuclear substitutions generally destroy activity, although some nuclear-substituted sulfathiazoles are said to be more potent than sulfathiazole. The class of *N*<sup>1</sup>-monosubstituted derivatives includes the most potent compounds, but the character of the substituent influences the degree of activity. Alkyl groups usually decrease activity, as do most aryl groups. The antibacterial action of *N*<sup>1</sup>-(3,5-dichlorophenyl)sulfanilamide against certain Gram-negative organisms, but not against Gram-positive species, is completely reversed by *p*-aminobenzoic acid (29).

*N*<sup>1</sup>-Acylsulfanilamides, especially those derived from straight-chain aliphatic acids, tend to be similar to sulfanilamide in activity, probably because of cleavage to sulfanilamide. Some of the methylated benzoyl derivatives, such as *N*<sup>1</sup>-(3,4-dimethylbenzoyl)sulfanilamide, are reported to be more active than sulfanilamide.

The *N*<sup>1</sup>-heterocyclic derivatives, especially those having two hetero atoms in the ring, such as two nitrogens or nitrogen and sulfur, are the most potent and useful derivatives. However, both the type of heterocycle and the substituents on it influence activity considerably. The differences in activity are not always readily explainable by theories concerning the mode of action. Where both *N*<sup>1</sup>-positions are substituted, considerably weaker activity results, possibly because of inability to ionize.

The *N*<sup>4</sup>-substituted sulfanilamides that are active are probably degraded in the body to the free 4-amino derivatives. The 4-nitrobenzenesulfonamides also depend for their activity upon conversion to the 4-amino derivatives by reduction *in vivo*.

*p*-(Aminomethyl)benzenesulfonamide depends for its activity upon another mechanism than *p*-aminobenzoic acid antagonism (27, p. 252).

#### TOXICITY

A small percentage of patients treated with sulfa drugs developed such symptoms of toxicity as drug fever, rashes, mild peripheral neuritis, and mental disturbances. Somewhat more common, especially when fluid intake is low, are the toxic symptoms which develop because of mechanical blockage in the kidneys from crystallization of the drug or its acetyl derivatives. This toxicity may be avoided in most cases by increased fluid intake and alkalization by administration of sodium bicarbonate.

More recently the principle of mixed sulfa drugs has been used to reduce this last type of toxicity (15,21,26,72,73). The therapeutic efficacy of a mixture is equal to the sum of the components, but there is much less danger of crystallization in the kidneys because the total solubility of the individual components and their acetyl derivatives is practically equal to the sum of the individual solubilities. For example, the combined solubilities of the three sulfa drugs sulfadiazine, sulfamerazine, and sulfamethazine (*meth-dia-mer-sulfonamides*, N.N.R.) with their acetyl compounds are then greater than that of one of the more soluble sulfa drugs, sulfisoxazole, plus its acetyl derivative, at a pH of less than 5.7, in a buffered solution at 37°C. (3). Since the pH of urine especially in illness is often 5.5 or less, this margin of safety in treatment is available when sulfa drug mixtures are used.

#### Analysis and Identification

For most of the sulfa drugs having a free 4-amino group, assay is readily carried out by titration with nitrous acid (20,36). Early methods involved a bromometric method (10). In assaying for sulfa drugs in body fluids, the Bratton-Marshall (4) method is used. The basis for this method is the diazotization of the aromatic amine group, followed by coupling with *N*-naphthylethylenediamine, and estimating colorimetrically the water-soluble dye.

The individual sulfa drugs are identified by procedures involving the heating of small samples and observing melting points (1), odors and colors (28), and by the

type or color of precipitates formed in alkaline solutions of the sulfa drug treated with copper sulfate solution (36).

The optical crystallographic properties of the crystalline sulfa drugs or certain other derivatives serve as another means of identification. See Table II. Special procedures are described for the assay of tablets (10,36).

The use of various mixtures of sulfa drugs has added to the difficulties of assay and identification. Chromatographic separations on paper using 1-butanol-ammonia (22,32), sodium hydroxide-methanol (34), or 1-butanol-acetic acid systems have been used along with assay by conventional methods or by color reactions (31). Separations have been made using ion-exchange chromatography in combination with radioactive techniques (6,16).

### Formulations and Uses

The sulfa drugs are usually administered orally either in the form of tablets or in suspensions of finely divided powder. When more rapid action is required, as in severe infection, solutions of the sodium salts are injected intravenously in order to obtain promptly adequate blood concentrations of the drugs.

The sulfa drugs have been successfully used to treat many types of infections such as those caused by  $\beta$ -hemolytic streptococci, pneumococci, staphylococci, gonococci, or meningococci.

Those drugs that are poorly absorbed, such as phthalylsulfathiazole and succinyl-sulfathiazole, are used mainly for treatment of infections of the gastrointestinal tract. Sulfaguanidine, although fully effective and completely absorbed in small doses, is incompletely absorbed in larger doses, and thus is also useful in the treatment of gastrointestinal infections.

Use has been made of sterile crystalline sulfa drugs or ointments in local infections, especially during World War II, but in general, topical application in wounds, burns, or superficial infections is contraindicated (26). *p*-(Aminomethyl)benzenesulfonamide, which is not an antagonist of *p*-aminobenzoic acid, has been widely used in the treatment of gas gangrene and tetanus (15,27, p. 252).

Mixtures of sulfa drugs are being used to overcome mechanical blockage of the kidneys (see p. 282).

Sulfaguanidine, sulfathiazole, sulfamethazine, and sulfapyridine are among those most often used in the veterinary field. Sulfaquinoxaline, which is not used in human therapy, is useful mainly in the poultry field, often being mixed with feed.

In general, the sulfa drugs have not shown significant effect in treatment of viral or protozoal infections or fungus diseases. See also *Malaria chemotherapy*, Vol. 8, p. 675.

### Bibliography

- (1) Baird, J. H., and Frediani, A. A., *J. Am. Pharm. Assoc., Sci. Ed.*, **39**, 273-74 (1950).
- (2) Bell, P. H., and Roblin, R. O., Jr., *J. Am. Chem. Soc.*, **64**, 2905-917 (1942).
- (3) Biamonte, A. R., and Schneller, G. H., *J. Am. Pharm. Assoc., Sci. Ed.*, **41**, 341-45 (1952).
- (4) Bratton, A. C., and Marshall, E. K., *J. Biol. Chem.*, **128**, 537-50 (1939).
- (5) Burger, A., *Medicinal Chemistry*, Interscience, New York-London, 1951, Vol. II.
- (6) Byrne, P. J., Jr., Alberts, A. A., and Christian, J. E., *J. Am. Pharm. Assoc., Sci. Ed.*, **42**, 77-79 (1953).
- (7) Castle, R. N., *J. Am. Pharm. Assoc., Sci. Ed.*, **40**, 162-3 (1951).

- (8) Castle, R. N., and Witt, N. F., *J. Am. Chem. Soc.*, **68**, 64-66 (1946).
- (9) Castle, R. N., Witt, N. F., and Poe, C. F., *J. Am. Chem. Soc.*, **71**, 228-31 (1949).
- (10) Conway, H. S., *J. Am. Pharm. Assoc., Sci. Ed.*, **34**, 236-37 (1945).
- (11) Ellingson, R. C., *J. Am. Chem. Soc.*, **63**, 2524-525 (1941).
- (12) Fildes, P., *Lancet*, **1940**, **I**, 955-7.
- (13) Grove, D. C., and Kennan, G. L., *J. Am. Chem. Soc.*, **63**, 97-99 (1941).
- (14) Hata, J., Yamada, S., Iwao, J., Kato, N., Sugimoto, N., and Inouye, R., *J. Pharm. Soc. Japan*, **69**, 477-79 (1949); *C.A.*, **44**, 3455 (1950).
- (15) Hawking, F., and Lawrence, J. S., *The Sulphonamides*, Grune and Stratton, N.Y., 1951.
- (16) Hutchins, H. H., and Christian, J. E., *J. Am. Pharm. Assoc., Sci. Ed.*, **42**, 310-14 (1953).
- (17) Keenan, G. L., *J. Am. Pharm. Assoc., Sci. Ed.*, **37**, 202-03 (1948).
- (18) King, V. L., and Parker, R. P., *FIAT Final Rept.*, **915**.
- (19) Krebs, H. A., and Speakman, J. C., *Brit. Med. J.*, **1946**, **I**, 47-50.
- (20) LaRocca, J. P., and Waters, K. L., *J. Am. Pharm. Assoc., Sci. Ed.*, **39**, 521-23 (1950).
- (21) Lehr, D., *Proc. Soc. Exptl. Biol. Med.*, **64**, 393-401 (1947).
- (22) Longenecker, W. H., *Anal. Chem.*, **21**, 1402-405 (1949).
- (23) Loop, W. von, and Lührs, E., *Ann.*, **580**, 225 (1953).
- (24) McCrone, W. C., and Johnson, R., *Anal. Chem.*, **21**, 1293-294 (1949).
- (25) N.F. IX, 1950.
- (26) N.N.R.—1954.
- (27) Northey, F. H., *The Sulfonamides and Allied Compounds*, Reinhold, N.Y., 1948.
- (28) Raybin, H. W., *J. Am. Pharm. Assoc., Sci. Ed.*, **34**, 196 (1945).
- (29) Roblin, R. O., Jr., *Chem. Revs.*, **38**, 255-377 (1946).
- (30) Schmidt, I. G., *J. Pharmacol. Exptl. Therap.*, **81**, 17 (1944).
- (31) Shepherd, R. G., *Anal. Chem.*, **20**, 1150-153 (1948).
- (32) Shepherd, R. G., *Proc. Scientific and Medicinal Conferences, Am. Pharm. Mfrs.' Assoc., 42nd Ann. Meeting, 1949*, pp. 30-35.
- (33) Sjögren, B., and Ortenblad, B., *Acta Chem. Scand.*, **1**, 605-81 (1947); *C.A.*, **42**, 4425 (1948).
- (34) Takagi, S., Suzuki, T., and Inaada, K., *Japan. J. Pharm. & Chem.*, **22**, 145 (1950); *C.A.*, **45**, 4884 (1951).
- (35) U.S.D., 24th ed., 1947, Supplement, 1950.
- (36) U.S.P. XIV, 1950.
- (37) Wejlard, J., Tishler, M., and Erickson, A. E., *J. Am. Chem. Soc.*, **66**, 1957-959 (1944).
- (38) White, B. J., Witt, N. F., Biles, J. A., and Poe, C. F., *Anal. Chem.*, **22**, 950 (1950).
- (39) Wilkerson, A. S., *J. Am. Chem. Soc.*, **64**, 2230 (1942).
- (40) Woods, D. D., *Brit. J. Exptl. Pathol.*, **21**, 74-90 (1940).
- (41) Woods, D. D., *Ann. N.Y. Acad. Sci.*, **52**, 1199-211 (1950).
- (42) Woolley, D. W., *A Study of Antimetabolites*, Wiley, N.Y., 1952.
- (43) Brit. Pat. 569,157 (May 10, 1945), G. A. Tuey (to Imperial Chemical Industries).
- (44) Brit. Pat. 609,571 (Oct. 4, 1948), Société des Usines Chimiques Rhône-Poulenc.
- (45) U.S. Pat. 2,085,037 (June 29, 1937), F. Mietzsch and J. Klarer (to Winthrop Chemical Co.).
- (46) U.S. Pat. 2,218,490 (Oct. 15, 1940), P. S. Winnek (to American Cyanamid Co.).
- (47) U.S. Pat. 2,275,354 (Mar. 3, 1942), A. J. Ewins and M. A. Phillips (to May & Baker Ltd.).
- (48) U.S. Pat. 2,288,531 (June 30, 1942), J. Klarer (to Winthrop Chemical Co.).
- (49) U.S. Pat. 2,324,013 (July 13, 1943), M. L. Moore (to Sharp & Dohme, Inc.).
- (50) U.S. Pat. 2,324,014 (July 13, 1943), M. L. Moore (to Sharp & Dohme, Inc.).
- (51) U.S. Pat. 2,324,015 (July 13, 1943), M. L. Moore (to Sharp & Dohme, Inc.).
- (52) U.S. Pat. 2,332,906 (Oct. 26, 1943), Z. Földi, I. Demjen, A. Gerecs, and R. König (to Alien Property Custodian).
- (53) U.S. Pat. 2,351,333 (June 13, 1944), H. Gysin (to J. R. Geigy, A.G.).
- (54) U.S. Pat. 2,362,087 (Nov. 7, 1944), G. Newberry (to May & Baker, Ltd.).
- (55) U.S. Pat. 2,386,852 (Oct. 16, 1945), M. Hartmann, F. Cueni, J. Druey, and H. von Meyenburg (to Ciba Pharmaceutical Products, Inc.).
- (56) U.S. Pat. 2,404,199 (July 16, 1946), J. Wejlard and M. Tishler (to Merck & Co., Inc.).
- (57) U.S. Pat. 2,407,966 (Sept. 17, 1946), J. M. Sprague (to Sharp & Dohme, Inc.).
- (58) U.S. Pat. 2,410,793 (Nov. 5, 1946), P. S. Winnek and R. O. Roblin, Jr. (to American Cyanamid Co.).

- (59) U.S. Pat. 2,411,495 (Nov. 19, 1946), M. Dohrn and P. Diedrich (to Schering Corporation).
- (60) U.S. Pat. 2,414,403 (Jan. 14, 1947), R. Winterbottom (to American Cyanamid Co.).
- (61) U.S. Pat. 2,417,005 (Mar. 4, 1947), H. Martin and F. Häfliger (to J. R. Geigy, A.G.).
- (62) U.S. Pat. 2,420,703 (May 20, 1947), R. C. Ellingson (to Mead Johnson and Co.).
- (63) U.S. Pat. 2,423,976 (July 15, 1947), M. E. Hultquist and E. H. Northey (to American Cyanamid Co.).
- (64) U.S. Pat. 2,429,184 (Oct. 14, 1947), M. Hartmann, H. von Meyenburg, and J. Druey (to Ciba Pharmaceutical Products, Inc.).
- (65) U.S. Pat. 2,430,094 (Nov. 4, 1947), H. M. Wuest and M. Hoffer (to Hoffmann-La Roche, Inc.).
- (66) U.S. Pat. 2,435,002 (Jan. 27, 1948), M. Hartmann and H. von Meyenburg (to Ciba Pharmaceutical Products, Inc.).
- (67) U.S. Pat. 2,443,742 (June 22, 1948), W. Lorenz, F. Behnisch, and F. Mietzsch (to Winthrop-Stearns, Inc.).
- (68) U.S. Pat. 2,444,012 (June 22, 1948), E. H. Northey and J. S. Webb (to American Cyanamid Co.).
- (69) U.S. Pat. 2,454,104 (Nov. 16, 1948), W. B. Tarply and A. I. Ryer (to Schering Corp.).
- (70) U.S. Pat. 2,476,655 (July 19, 1949), H. Fox, P. Diedrich, and M. Dohrn (to Schering Corp.).
- (71) U.S. Pat. 2,482,085 (Sept. 20, 1949), M. N. Dvornikoff (to Monsanto Chemical Co.).
- (72) U.S. Pat. 2,484,174 (Oct. 11, 1949), D. Lehr.
- (73) U.S. Pat. 2,484,175 (Oct. 11, 1949), D. Lehr.
- (74) U.S. Pat. 2,488,081 (Nov. 15, 1949), M. L. A. Fluchaire and S. Javorsky (to Société des Usines Chimiques Rhône-Poulenc).
- (75) U.S. Pat. 2,497,163 (Feb. 14, 1950), M. L. A. Fluchaire and G. L. A. Bost (to Société des Usines Chimiques Rhône-Poulenc).
- (76) U.S. Pat. 2,508,929 (May 23, 1950), H. H. Richmond (to U.S. Rubber Co.).
- (77) U.S. Pat. 2,513,999 (July 4, 1950), C. F. Jelinek (to General Aniline and Film Corp.).
- (78) U.S. Pat. 2,592,859 (April 15, 1952), T. F. Cleary, Jr. (to E. R. Squibb and Sons).
- (79) U.S. Pat. 2,592,860 (April 15, 1952), T. F. Cleary, Jr. (to E. R. Squibb and Sons).

M. E. HULTQUIST

**SULFAMATION.** See *Sulfonation and sulfation*.

## SULFAMIC ACID

Sulfamic acid (amidosulfuric acid, aminosulfuric acid),  $\text{NH}_2\text{SO}_2\text{OH}$  or  $\text{HOSO}_2\text{NH}_2$ , formula weight 97.098, is the monoamide of sulfuric acid. It was a laboratory curiosity for nearly one hundred years until new and practical methods of manufacture were discovered in 1936. Rose is credited with the first actual preparation about 100 years before this, and later E. Berglund prepared the pure acid. Sulfamic acid is commercially produced by the reaction between urea, sulfur trioxide, and sulfuric acid.

Several unusual characteristics have facilitated its rapid acceptance in various industrial uses. Although a very strong acid in water solution, sulfamic acid may be handled as an easily transported, stable, crystalline solid. The acid and its salts are used as flame retardants, weed killers, metal cleaners, and electroplating salts.

### Properties

The most outstanding physical property of the acid is its stability as a dry, non-hygroscopic, odorless, colorless, crystalline material. The crystals may be kept for years in the laboratory without change and are a convenient standard for titrimetry. Some physical properties are given below (see also refs. 16,28):

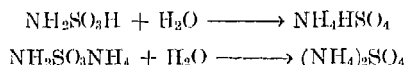
M.p.	205°C.
Density	2.126 g./cu.cm.
Limiting conductance (sulfamate ion)	48.59
Dissociation constant at 25°C.	$1.01 \times 10^{-1}$
Refractive indexes (25°±3°C.)	
$\alpha$	1.553
$\beta$	1.563
$\gamma$	1.568

Although easy to handle dry, the acid is highly ionized in solution and is comparable with the common strong acids. The pH of a 1% solution is 1.18 (see also ref. 9a). Sulfamic acid is moderately soluble in water, 14.68 grams dissolving in 100 grams of water at 0°C. and 47.08 grams at 80°C. (9a). It is soluble in formamide and practically insoluble in 70–100% sulfuric acid and in various organic liquids.

Sulfamic acid crystallizes in the orthorhombic system with a unit cell of 8 molecules. Tablets and compact prisms are obtained from cold aqueous solutions, large, lozenge-shaped plates on cooling hot aqueous solutions.

**Inorganic Reactions.** Sulfamic acid starts to decompose at 209°C. and at 260°C. it produces sulfur dioxide, sulfur trioxide, nitrogen, water, and other products.

At room temperature dilute aqueous solutions of sulfamic acid are stable for many months. At higher temperatures hydrolysis of the acid and its ammonium salt is comparatively rapid, forming ammonium hydrogen sulfate and ammonium sulfate, respectively, as follows:



The rate of hydrolysis is a function of the concentration, temperature, and pH (9a). At 80°C., 43.66% hydrolysis occurs in a 10% solution at the end of 8 hours. The pH is a very important factor with ammonium sulfamate; for example, a 60% aqueous solution of ammonium sulfamate, at a pH of 5, will begin "runaway" hydrolysis at 200°C., and at a pH of 2 at only 130°C.

Under such special conditions, if a concentrated aqueous solution of ammonium sulfamate is heated in a closed container, or in one with a very small vent, the spontaneous hydrolysis, which is strongly exothermic, can generate sufficient steam pressure to cause an explosion (13). Amine salts (see pp. 288,290) behave similarly.

Under ordinary conditions of use, there appears to be no danger from rapid hydrolysis. Solutions of ammonium sulfamate will not have a pH lower than about 4.5 at concentrations of 60% or above, unless acid is added, and if solutions are stored in open containers the temperature will not rise above the boiling point, which for a 60% solution is approximately 107°C.

Maron and Berens (20) suggest a mechanism for the hydrolysis which involves the formation of an intermediate dipolar ion in equilibrium with the reactants. This may explain the high values for the energy and the entropy of activation:

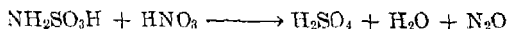
$$\Delta H = 29,800 \text{ calories, } \Delta S = 9.69 \text{ entropy units}$$

In liquid ammonia, sulfamic acid behaves as a dibasic acid, one hydrogen of the amino group being replaceable by Na, K, etc., giving salts of the formula  $\text{NaNH}_2\text{SO}_3\text{Na}$ , etc.

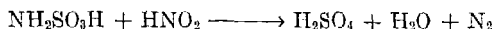
Chlorine, bromine, and chlorates oxidize sulfamic acid to sulfuric acid and nitrogen.

Hypochlorous acid at low temperature is reported to form unstable *N*-chloro derivatives.

Pure nitrous oxide is obtained by the reaction of concentrated nitric acid with sulfamic acid:



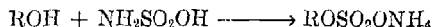
Nitrous acid reacts very rapidly and quantitatively with sulfamic acid, yielding nitrogen gas:



This is the most outstanding inorganic reaction of sulfamic acid and it is utilized industrially to destroy nitrites in the manufacture of dyes, in the purification of hydrochloric and sulfuric acids (49), and in the determination of biochemical oxygen demand in sewage treatment.

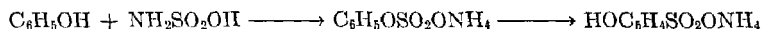
**Organic Reactions.** Audrieth and co-workers have thoroughly reviewed the organic reactions of sulfamic acid (2).

Primary alcohols react with sulfamic acid to form alkyl ammonium sulfates:



Secondary alcohols react in the presence of an amide catalyst such as acetamide or urea, but tertiary alcohols do not react (12,61).

Phenol, cresols, xyenols, naphthols, pyrocatechol, resorcinol, hydroquinone, anisole, phenetole, and phenyl ether are sulfonated when treated with sulfamic acid. In most instances, aryl ammonium sulfates are formed as intermediates and the sulfonate results from a subsequent rearrangement. Thus with phenol:



Phenyl derivatives such as anethole, styrene, and isosafrole with unsaturated alkyl side chains are sulfonated in the side chain by reaction with sulfamic acid.

Amides react in certain cases to form ammonium salts of sulfonated amides. For example, treatment with benzamide yields the ammonium salt of *N*-benzoylsulfamic acid,  $\text{C}_6\text{H}_5\text{CONHSO}_2\text{ONH}_4$ , and with ammonium sulfamate it yields diammonium imidodisulfonate,  $\text{HN}(\text{SO}_2\text{ONH}_4)_2$ .

Aldehydes form addition products with sulfamic acid salts. These are stable in neutral or slightly alkaline solutions, but are hydrolyzed in acid and strongly alkaline solutions. With formaldehyde, the salt of the methylol (hydroxymethyl) derivative,  $\text{Ca}(\text{O}_3\text{SNHCH}_2\text{OH})_2$ , is readily obtained as a crystalline solid.

Cadmium, cobalt, copper, and nickel sulfamates react with lower aliphatic aldehydes (22). These stable compositions are reported to be suitable for use in electroplating solutions for deposition of the respective metals.

Guanylurea sulfamate is prepared by hydrolysis of dicyanodiamide with sulfamic acid in the presence of water (42). Amidine sulfamates such as guanidine sulfamate are prepared by the addition of guanidine to sulfamic acid. Urea and ammonium sulfamate react to form guanidine sulfate. The same reactants (32) heated at 250–400°C. are reported to give melamine (42,62). See Vol. 1, p. 744; *Guanidine*; *Urea*.

The *N*-alkyl and -cyclohexyl derivatives of sulfamic acid are comparatively stable and may be isolated; the *N*-aryl derivatives are very unstable and can only be obtained in the form of their salts. A series of stable thiazolylsulfamic acids has been prepared.

Sulfation by sulfamic acid has been used, especially in Germany, in the preparation of detergents from dodecyl, oleyl, and other higher alcohols (61). Secondary alcohols may be sulfated readily by addition of pyridine. See *Sulfonation and sulfation*.

Cellulose sulfated with sulfamic acid shows less degradation than the customary product from sulfuric acid (67). Cellulose esters of sulfamic acids are formed by the reaction of sulfamyl halides in the presence of tertiary organic bases.

#### PROPERTIES OF SALTS OF SULFAMIC ACID

Sulfamic acid readily forms the various metal sulfamates by reaction with the respective oxides, hydroxides, carbonates, or active metals. With the exception of the basic mercury salt, its salts are very soluble, particularly the lead salt.

Precise solubility determinations are available for only a few salts (25). The solubility of sodium sulfamate (17) has been determined from 0 to 55°C. At 0°C., 79.90 grams dissolve in 100 grams of water; at 55°C., 191.30 grams dissolve. The solid phase in equilibrium with the saturated solution below the transition point, 38.3°C., is the monohydrate, a waxy, difficultly filterable material; above the transition point the anhydrous salt is formed. The anhydrous salt melts at 250°C.

Ammonium sulfamate is five times as soluble in water as ammonium chloride (200.2 grams dissolve in 100 grams of water at 20°C.) and very soluble in glycerol, glycols, and formamide. The pH of a 5% (0.44 *N*) solution is 5.2. Ammonium sulfamate melts at 132.9°C.

Ammonium sulfamate and sodium sulfamate form  $2\text{NH}_4\text{O}_3\text{SNH}_2 \cdot 5\text{NaO}_3\text{SNH}_2$ , melting at 213°C. This compound forms a eutectic composition with ammonium sulfamate at 118.8°C. (the melt containing 16.95% sodium sulfamate) and with sodium sulfamate at about 212°C. (containing 73% sodium sulfamate) (18).

Ricci and Selikson (25) found no evidence of solid solutions or double compounds in the system  $\text{NH}_4\text{O}_3\text{SNH}_2\text{--NH}_2\text{SO}_3\text{H--H}_2\text{O}$ .

King and Hooper (15) give comprehensive tables of solubilities for calcium, barium, and magnesium salts from 0 to 100°C.

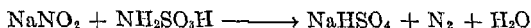
The relative viscosity and relative density of aqueous solutions of the acid and the ammonium, magnesium, calcium, and barium salts have been determined for several concentrations at 25°C. (26).

Lead sulfamate gives solutions with high densities (2.18 at 68.5%) which may be used for determining the density of heavy solids.

A series of substituted ammonium sulfamates is formed by direct reaction of the acid with the appropriate primary, secondary, or tertiary amines, including ethanol amines and other hydroxy amines (8). All of these salts are usually soluble in water, alcohol, dilute methanol, formamide, and polyhydric alcohols. They are insoluble in ether.

#### Analysis

Sulfamic acid or the sulfamate ion may be quantitatively determined by reaction with nitrite ion:



Bowler and Arnold (6) utilized this reaction in a rapid direct titration method using a starch-iodide external indicator. Accuracy was comparable with that of the older

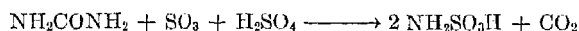


gravimetric methods involving oxidation of sulfamate to sulfate. A gasometric method (9) depending on measurement of the nitrogen evolved can be performed with simple apparatus or can be adapted to micro procedures where the accuracy is  $\pm 5\%$  and the operation requires only 20 minutes. The reaction is specific for the amino group and very few ions interfere.

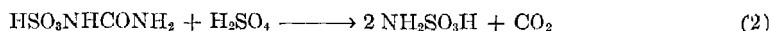
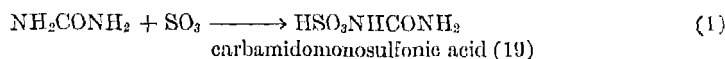
Sulfamic acid and its salts retard the precipitation of barium sulfate. To accurately determine traces of sulfate derived from hydrolysis of sulfamic acid it is essential to let the barium sulfate precipitate stand over night.

### Manufacture

Sulfamic acid is manufactured by the reaction of equimolal quantities of urea, sulfur trioxide, and sulfuric acid (51-54), a modification of the process discovered independently by Baumgarten (4,33) and Cupery (37). The reaction, which is strongly exothermic, may be represented stoichiometrically:



The reaction is considered theoretically to take place in two steps:



Excess liquid sulfur trioxide may be used as a reaction medium (59). A liquid mixture of equimolar quantities of urea and sulfuric acid is added to a large excess of liquid sulfur trioxide while agitating and cooling to prevent carbon dioxide formation. After completion of the initial reaction, the mass is heated further to produce sulfamic acid. The excess sulfur trioxide is removed by distillation or spray drying, or both, or by flaking.

Sulfamic acid may also be prepared by reaction between chlorosulfonic acid and urea (34) and by reaction of sulfur dioxide with hydroxylamine (43) or with acetoxime (27,43), or by the anhydrous reaction of sulfur trioxide and ammonia (28a).

The salts of sulfamic acid are manufactured by neutralizing the acid with the appropriate hydroxide or carbonate. Ammonium sulfamate is the most important commercial salt. It is manufactured by adding anhydrous ammonia and sulfamic acid to ammonium sulfamate mother liquor from a preceding crystallization until a hot, concentrated ammonium sulfamate solution is formed (64). The anhydrous ammonia is added slowly with agitation, while the heat of reaction is removed by cooling coils. The hot, concentrated ammonium sulfamate solution is then run to crystallizers from which ammonium sulfamate crystals are recovered, while the cold mother liquor is returned to the neutralization step.

Kamlet (68) has described a direct route to ammonium sulfamate wherein a tertiary amine-sulfur trioxide complex (for example, pyridine-sulfur trioxide) is treated with ammonia in excess tertiary amine.

Sulfamic acid technical (minimum analysis 97.0%) is packaged in 400-lb. fiber drums. Its price (car- or truckloads) was \$0.15 per pound., f.o.b., Grasselli, N.J., in August 1954.

Ammonium sulfamate technical, minimum analysis 98.5%, is packaged in lined paper bags, 100 lb. each. Its price (car- or truckloads) was \$0.18 per pound f.o.b., Grasselli, N.J., in August 1954.

### Health and Safety Factors

Although dry crystalline sulfamic acid causes no noticeable ill effect upon brief contact with the skin, precautions should nevertheless be taken to avoid contact with the eyes, skin, or clothing since it becomes a highly ionized acid in contact with water. The main effect of sulfamic acid is a local irritation to the skin or mucous membrane due to its acidity which is comparable to other inorganic acids. Safety goggles and a respirator should be worn when handling the dry acid to protect against flying particles.

When handling solutions, protection against ingestion, spills, and splashes is of the same importance as in handling solutions of the more common inorganic acids such as hydrochloric and sulfuric. Ingestion of moderate doses has no systemic toxic effect apart from the irritant action common to strong inorganic acids (1).

Ammonium sulfamate like the more common ammonium salts such as the chloride or sulfate is neither very irritant to the skin nor very toxic. Care should be exercised in heating solutions of sulfamic acid, or ammonium sulfamate, especially in closed containers or those with only a small vent, since a dangerous "runaway" hydrolysis may occur, particularly with the ammonium salt. Under some conditions an explosion may result (see p. 286).

### Uses

*Analytical Uses.* Sulfamic acid has been recommended as a standard of reference in acidimetry (7). The acid is readily purified by recrystallization and air drying to give a stable product analyzing 99.95%. A variety of indicators are suitable; bromothymol blue gives a sharp change from yellow at pH 6.4 to blue at pH 7.0.

The procedure for the determination of sulfamic acid with nitrite has been adapted in reverse for the determination of nitrite ion. Sulfamic acid improves the Winkler method for determining dissolved oxygen in water by removing interfering nitrites. Sulfamic acid is used for removal of nitrites in the Marshall procedure for determining the sulfanilamide content of blood.

*Fire Retardants.* The sulfamates are highly compatible with cellulose and are extensively used as fire-retarding agents (35,60). Ammonium sulfamate is unique among ordinary fire retardants as it does not cause stiffening or otherwise adversely affect the hand and feel of paper and fabrics. The sulfamates show no tendency to crystallize on the surface of the flameproofed article on aging. Wearing apparel treated with ammonium sulfamate retains its original appearance and texture.

Flameproofed draperies which are often exposed to wide variations in temperature and humidity show no efflorescence of the sulfamate upon the surface of the fabric. Under certain special conditions where a slight afterglow cannot be tolerated or where exceptionally high humidities are encountered, modified compositions of ammonium sulfamate are recommended. See *Fire-resistant textiles*.

Sulfamate fire retardants are now being used for flameproofing service clothing, drapes, curtains, decorative material, blankets, and wearing apparel.

*Softening Agents.* Certain amine salts of sulfamic acid have been found to have outstanding properties as softeners for paper and textiles (5,69). Compared with other commonly used softening agents, their softening action is longer lasting and is better at low humidities. Indications are the amine salts do not depend entirely on moisture pickup for their softening action.

The mono-, di-, and triethanolamine sulfamates (2-hydroxyethylammonium sulfamates, as,  $\text{NH}_2\text{SO}_2\text{ONH}_3(\text{CH}_2\text{CH}_2\text{OH})$ , see *Ethanolamines*) and the mono- and diisopropanolamine sulfamates (2-hydroxypropylammonium sulfamates, as,  $\text{NH}_2\text{SO}_2\text{ONH}_3(\text{CH}_2\text{CHOHCH}_3)$ , see *Propanolamines*) are the most stable and give the best softening action. Resistance of treated paper and textiles to yellowing is generally good but can be further improved by the use of small amounts of buffers, such as tri-sodium phosphate or sodium acetate, and mild reducing agents such as sodium hypophosphite, urea, or sodium sulfite.

Treatment of articles to be softened is accomplished by simple processes and the degree of softness obtained increases with increasing retentions of the amine sulfamate. The amine sulfamates have been applied widely to paper draperies and their unique properties suggest their use as softening agents for other paper products.

*Weed and Brush Killers.* Sulfamic acid and certain of its salts have proved to be highly effective weed killers (*q.v.*) (11,45,50). Ammonium sulfamate is a nonselective killer for weeds, brush, stumps, and trees.

*Metal Cleaning.* Sulfamic acid is utilized by the sugar industry in removing scale from heat-transfer coils. The ease of handling the powdered dry composition and the reduced corrosion balance the price differential over the common acids. On many metals sulfamic acid solutions have been found to be markedly less corrosive than solutions of sulfuric or hydrochloric acids (see Table I). In the dairy industry, milkstone is rapidly dissolved, probably due to the solubility of calcium sulfamate. Carbonate scales are generally more rapidly dissolved by sulfamic acid than by other acids. Wire-drawing compounds are readily removed by sulfamate cleaning solutions.

TABLE I. Relative Corrosion Rates of 3% Aqueous Solutions of Acids at  $72^\circ \pm 4^\circ\text{F}$ . Sulfamic Acid = 1.0.

Metal	$\text{H}_2\text{SO}_4$	HCl
1010 Steel	2.6	4.2
Cast iron	3.2	3.2
Galvanized iron	63.0	VR <sup>a</sup>
Tin plate	81.0	23.
304 stainless	10.0	VR <sup>a</sup>
Zinc	2.2	VR <sup>a</sup>
Copper	1.5	6.7
Brass	1.5	2.8
Bronze	4.0	7.0
Aluminum	0.6	5.3

<sup>a</sup>VR = very rapid corrosion.

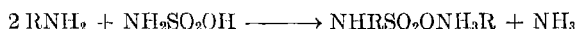
*Dye Industry.* The quantitative reaction of sulfamic acid with nitrites is utilized in the dye industry for the removal of the excess nitrite required for the diazotization reaction. In dyeing piece goods, the color may be developed directly on the fabric. With the rapid and convenient removal method afforded by sulfamate, it is possible to employ greater excesses of nitrite, thus facilitating dye development. Since the reaction can be closely controlled, greater dye uniformity and cleaner shades of color result. One of the first industrial uses of sulfamic acid was in the removal of excess nitrites in the process of dyeing leather with a developable azo dye (36).

Sulfamic acid and its salts can be used to stabilize certain diazo compositions (46). Aromatic diamino compounds, such as *o*-diaminobenzene and 1,5-diaminonaphthalene,

are treated with chlorosulfonic acid to introduce sulfo groups. One sulfo group is removed during diazotization with nitrous acid leaving a monodiazosulfamic acid suitable for coupling with 2-naphthol to yield a soluble azo dye.

*Electroplating.* The ready solubility of many sulfamate salts suggests their usefulness as electroplating salts (23,24). Nickel, copper, and lead may be electro-deposited from solutions of their sulfamates and give very smooth coatings (47). The deposition of nickel coatings is utilized in the precise duplication of electrotypes. Sulfamic acid has been used in a plating bath for indium. See Vol. 7, p. 837.

*Sweetening Agents (q.v.).* The cyclohexylsulfamates were accidentally discovered to possess a high degree of sweetness (44). They may be used freely and do not leave an unpleasant aftertaste or decompose in cooking. They can be prepared directly from sulfamic acid and cyclohexylamine or a substituted cyclohexylamine:



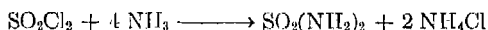
Treatment with sodium or calcium hydroxide gives the corresponding cyclohexyl-sulfamate, as  $\text{NHRSO}_2\text{ONa}$  (31).

*Other Uses.* Other possible applications for sulfamic acid and its derivatives are indicated especially in the patent literature (10,39,41,48,55,56,57,60,63,65,66,70).

### Derivatives

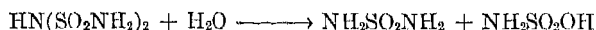
**Sulfamide**,  $\text{NH}_2\text{SO}_2\text{NH}_2$ , formula weight 96.108, a white, crystalline solid melting at  $93^\circ\text{C}$ ., was first obtained pure by Ruff in 1903 through the reaction of an excess of liquid ammonia with sulfuryl chloride. The compound is very stable in air and also in dilute acid or alkaline solutions. Boiling with strong alkali yields a sulfamate and continued boiling with hydrochloric acid causes a stepwise hydrolysis to sulfuric acid. Sulfamide is soluble in water and in liquid ammonia. It dissolves readily in concentrated nitric acid without reaction, but forms a monochlorosulfamide (m.p.  $66^\circ\text{C}$ .) with hypochlorous acid.

Theoretically sulfamide should be obtained through the reaction of ammonia and sulfuryl chloride:



Although various modifications of this procedure have been thoroughly investigated, it usually gives very poor yields, probably due to the formation of polymeric compounds such as  $\text{NH}_2(\text{SO}_2\text{NH})_n\text{SO}_2\text{NH}_2$ . When these are hydrolyzed, the major product is sulfamic acid with only a small portion of sulfamide.

Sulfuryl chloride and liquid ammonia in excess give imidodisulfamide,  $\text{HN}(\text{SO}_2\text{NH}_2)_2$ , as a main product. This could be hydrolyzed to give one mole of sulfamide for each mole of sulfamic acid:



Evaporation to dryness followed by extraction with ethyl acetate, in which sulfamic acid is insoluble, gives pure sulfamide.

A patent (51a) specifies injecting sulfuryl chloride into ammonia maintained at  $-78^\circ\text{C}$ . to  $+90^\circ\text{C}$ . under pressure.

The chemistry of sulfamide was thoroughly reviewed by Audrieth and co-workers (2). Paquin (22a) reported his extensive investigation of the reactions of sulfamide

with alcohols, organic acids, and aldehydes. Reaction with amines gives compounds such as butylsulfamide, cyclohexyl sulfamide, and with aniline a diphenyl sulfamide. The reaction of sulfamide with formaldehyde gives a hard, water-clear resin which is insoluble in many organic solvents, but softens in water and dissolves completely on boiling. Structures analogous to urea resins (see *Amino resins*) have been postulated.

### Bibliography

- (1) Ambrose, A. M., *J. Ind. Hyg. Toxicol.*, **25**, 26-28 (1943).
- (2) Audrieth, L. F., Sveda, M., Sisler, H. H., and Butler, M. J., *Chem. Revs.*, **26**, 49-94 (1940).
- (3) Baumgarten, P., and Marggraff, I., *Ber.*, **63**, 1019-24 (1930).
- (4) Baumgarten, P., *Ber.*, **69**, 1929-37 (1936).
- (5) Blakemore, F. T., *Am. Paper Converter*, **23**, No. 6, 11, 29 (1949).
- (6) Bowler, W. W., and Arnold, E. A., *Anal. Chem.*, **19**, 336-37 (1947).
- (7) Butler, Sister M. J., Smith, G. F., and Audrieth, L. F., *Ind. Eng. Chem., Anal. Ed.*, **10**, 690-92 (1938).
- (8) Butler, S. M. J., and Audrieth, L. F., *J. Am. Chem. Soc.*, **61**, 914-15 (1939).
- (9) Carson, W. N., Jr., *Anal. Chem.*, **23**, 1016-19 (1951).
- (9a) Cupery, M. E., *Ind. Eng. Chem.*, **30**, 627-31 (1938).
- (10) Cupery, M. E., and Gordon, W. E., *Ind. Eng. Chem.*, **34**, 792-97 (1942).
- (11) Dietz, H. F., Vogel, M. A., and Cupery, H., *Agric. News Letter*, **9**, 35-39 (1941).
- (12) Divers, Ed., and Haga, T., *J. Chem. Soc.*, **69**, 1634-53 (1896).
- (13) Hunt, J. K., *Chem. Eng. News*, **30**, 707 (1952); *Chem. Week*, **69**, No. 11, 2, 4 (1951).
- (14) Jacobs, H. L., *Elec. Light Power*, **26**, No. 7, 62-64 (1948).
- (15) King, G. B., and Hooper, J. F., *J. Phys. Chem.*, **45**, 938-42 (1941).
- (16) King, E. J., and King, G. W., *J. Am. Chem. Soc.*, **74**, 1212-15 (1952).
- (17) Laning, S. H., and van der Meulen, P. A., *J. Am. Chem. Soc.*, **69**, 1828-30 (1947).
- (18) Laning, S. H., and van der Meulen, P. A., *J. Am. Chem. Soc.*, **70**, 1799-1800 (1948).
- (19) Linhard, M., *Ann.*, **535**, 267-84 (1938).
- (20) Maron, S. H., and Berens, A. R., *J. Am. Chem. Soc.*, **72**, 3571-74 (1950).
- (21) Meuwesen, A., and Merkel, H., *Z. anorg. u. allgem. Chem.*, **244**, 89-93 (1940).
- (22) Morin, E. A., and Choguill, H. S., *Trans. Kansas Acad. Sci.*, **53**, 212-16 (1950).
- (22a) Paquin, A. M., *Angew. Chem.*, **60**, 316-20 (1948).
- (23) Piontelli, R., *Korrosion u. Metallschutz*, **19**, 110-13 (1943).
- (24) Piontelli, R., *J. Electrochem. Soc.*, **94**, 106-8 (1948).
- (25) Ricci, J. E., and Selikson, B., *J. Am. Chem. Soc.*, **69**, 995-98 (1947).
- (26) Schmelzle, A. F., and Westfall, J. E., *J. Phys. Chem.*, **48**, 165-68 (1944).
- (27) Sisler, H. H., and Audrieth, L. F., *J. Am. Chem. Soc.*, **61**, 3389-91 (1939).
- (28) Taylor, E. G., Desch, R. P., and Catotti, A. J., *J. Am. Chem. Soc.*, **73**, 74-77 (1951).
- (28a) Uchida, S., and Yukio, I., *J. Chem. Soc. Japan, Ind. Chem. Sect.*, **53**, 423 (1950).
- (29) Brit. Pat. 577,988 (June 11, 1946), Sylvania Industrial Corp.
- (30) Brit. Pat. 647,316 (Dec. 13, 1950), Spolek pro Chemickou a Hutni Vyrobu, Narodni Podnik.
- (31) Brit. Pat. 662,800 (Dec. 12, 1951), Abbott Laboratories.
- (32) Can. Pat. 473,968 (May 29, 1951), J. S. Mackay (to American Cyanamid Co.).
- (33) U.S. Pat. 2,102,350 (Dec. 14, 1937), Paul Baumgarten (to Du Pont).
- (34) U.S. Pat. 2,109,952 (March 1, 1938), Max Wyler (to Imperial Chem. Industries, Ltd.).
- (35) U.S. Pat. 2,142,116 (Jan. 3, 1939), M. E. Cupery (to Du Pont).
- (36) U.S. Pat. 2,160,882 (June 6, 1939), H. A. Lubs (to Du Pont).
- (37) U.S. Pat. 2,191,754 (Feb. 27, 1940), M. E. Cupery (to Du Pont).
- (38) U.S. Pat. 2,195,419 (April 2, 1940), D. M. McQueen & M. T. Goebel (to Du Pont).
- (39) U.S. Pat. 2,212,152 (Aug. 20, 1940), M. E. Cupery (to Du Pont).
- (40) U.S. Pat. 2,232,241 (Feb. 18, 1941), L. C. Jones (to American Cyanamid Co.).
- (41) U.S. Pat. 2,236,513 (April 1, 1941), H. Bradshaw (to Du Pont).
- (42) U.S. Pat. 2,259,563 (Oct. 21, 1941), Wm. H. Hill (to American Cyanamid Co.).
- (43) U.S. Pat. 2,263,262 (Nov. 18, 1941), M. E. Cupery (to Du Pont).
- (44) U.S. Pat. 2,275,125 (March 3, 1942), L. F. Audrieth and M. Sveda (to Du Pont).
- (45) U.S. Pat. 2,277,744 (March 31, 1942), M. E. Cupery and A. P. Tanberg (to Du Pont).

- (46) U.S. Pat. 2,314,196 (March 16, 1942), E. W. Clark (to Allied Chemical & Dye Corp.).
- (47) U.S. Pat. 2,318,592 (May 11, 1943), M. E. Cupery (to Du Pont).
- (48) U.S. Pat. 2,343,326 (March 7, 1944), V. H. Reckmeyer and A. H. Brunner, Jr. (to General Aniline & Film Corp.).
- (49) U.S. Pat. 2,355,702 (Aug. 15, 1944), W. A. Brooks (to Du Pont).
- (50) U.S. Pat. 2,368,276 (Jan. 30, 1945), R. E. Torley (to American Cyanamid Co.).
- (51) U.S. Pat. 2,390,648 (Dec. 11, 1945), D. P. Hill and G. A. Peirce (to Du Pont).
- (51a) U.S. Pat. 2,407,481 (Sept. 10, 1946), E. J. Degering and G. C. Gross (to Purdue Research Foundation).
- (52) U.S. Pat. 2,408,492 (Oct. 1, 1946), E. J. Tauch (to Du Pont).
- (53) U.S. Pat. 2,408,823 (Oct. 8, 1946), E. J. Tauch (to Du Pont).
- (54) U.S. Pat. 2,409,572 (Oct. 15, 1946), J. W. Leonard (to Du Pont).
- (55) U.S. Pat. 2,415,169 (Feb. 4, 1947), A. G. Gray (to Du Pont).
- (56) U.S. Pat. 2,422,730 (June 24, 1947), W. A. Hoffman (to Du Pont).
- (57) U.S. Pat. 2,423,556 (July 8, 1947), R. Feibelman (to Heyden Chemical Corp.).
- (58) U.S. Pat. 2,426,420 (Aug. 26, 1947), E. J. Tauch (to Du Pont).
- (59) U.S. Pat. 2,436,658 (Feb. 24, 1948), H. S. McQuaid (to Du Pont).
- (60) U.S. Pat. 2,452,054 (Oct. 26, 1948), G. Jones and S. Soll (to Albi Mfg. Co.).
- (61) U.S. Pat. 2,452,943 (Nov. 2, 1948), J. D. Malkemus, J. R. Ramsay, and D. J. Potter (to Colgate-Palmolive-Peet Co.).
- (62) U.S. Pat. 2,464,247 (March 15, 1949), J. S. Mackay (to American Cyanamid Co.).
- (63) U.S. Pat. 2,482,755-756 (Sept. 27, 1949), F. M. Ford and W. P. Hall (to Jos. Bancroft & Son).
- (64) U.S. Pat. 2,487,480 (Nov. 8, 1949), C. A. Rohrmann (to Du Pont).
- (65) U.S. Pat. 2,493,444 (Jan. 3, 1950), J. R. Clark and J. D. Malkemus (to Colgate-Palmolive-Peet Co.).
- (66) U.S. Pat. 2,493,445 (Jan. 3, 1950), J. R. Clark, J. D. Malkemus, and J. Ross (to Colgate-Palmolive-Peet Co.).
- (67) U.S. Pat. 2,511,229 (June 13, 1950), J. C. Thomas (to Du Pont).
- (68) U.S. Pat. 2,514,955 (July 11, 1950), J. Kumlet (to Mathieson Chemical Corp.).
- (69) U.S. Pat. 2,526,462 (Oct. 17, 1950), O. Edelstein (to The Pond Lily Co.).
- (70) U.S. Pat. 2,586,287 (Feb. 19, 1952), L. D. Apperson and E. L. Richardson (to Colgate-Palmolive-Peet Co.).

GILBERTA G. TORREY

**SULFAMIDE**,  $\text{SO}_2(\text{NH}_2)_2$ . See *Sulfamic acid*.

**SULFANILAMIDE**,  $\text{C}_6\text{H}_4\text{N}_2\text{O}_2\text{S}$ . See *Sulfa drugs*.

**SULFANILIC ACID**,  $p\text{-H}_2\text{NC}_6\text{H}_4\text{SO}_3\text{H}$ . See *Aniline*, Vol. 1, p. 923.

**SULFARSPHENAMINE**,  $\text{C}_{14}\text{H}_{14}\text{As}_2\text{N}_2\text{Na}_2\text{O}_8\text{S}_2$ ; **SULFARSPHENAMINE BISMUTH**.  
See *Arsenic preparations*, Vol. 2, p. 127.

**SULFATASES**. See *Fermentation*, Vol. 6, p. 325.

**SULFATED ACIDS, ALCOHOLS, OILS, etc.** See *Sulfonation and sulfation; Surface-active agents*.

**SULFATE PROCESS**. See *Pulp*, Vol. 11, p. 262.

**SULFATES**. See such articles as *Ammonium compounds; Calcium compounds*. See also *Sulfuric and sulfurous esters*.

**SULFATION**. See *Sulfonation and sulfation*.

**SULFATO DYES**. See *Acetate dyes*, Vol. 1, p. 55.

**SULFENIC ACIDS**,  $\text{RSOH}$ ; **SULFENYL HALIDES**,  $\text{RSX}$ . See *Sulfur compounds, organic*.

**SULFHYDRYL (SULFHYDRIL) GROUP, —SH.** See *Mercaptans*, Vol. 8, p. 858.

**SULFIDE DYES.** See *Sulfur dyes*.

**SULFIDES, INORGANIC.** See such articles as *Ammonium compounds*; *Barium compounds*. See also *Sulfur compounds, inorganic*.

## SULFIDES, ORGANIC

The organic sulfides may be represented by the general formula  $R-S-R$  and hence resemble the ethers in certain properties; they are sometimes called *thioethers*. Examples of all types are known, where  $R$  and  $R'$  may be the same or different, and may be aliphatic, aromatic, or heterocyclic. Related to these compounds are the organic disulfides,  $R-S-S-R$ , which may be regarded as analogs of organic peroxides, and have some properties in common with these oxygen compounds. The term polysulfide is somewhat ambiguous, being used commonly for the compounds represented by the formula  $R-S_n-R$  where  $n$  is greater than 3, but "polysulfide" also refers to polymers of the Thiokol type,  $(-X-S_n-X-S_n-)_z$  (see Vol. 11, p. 842), where  $X$  is an organic biradical, and it is sometimes erroneously applied to polymers of the polyalkylene sulfide type,  $(-C_n-S-C_n-S-)_z$ . The field of organic sulfides has been reviewed by Connor (12).

For cyclic sulfides see *Heterocyclic compounds* and such articles as *Thiazole dyes*; *Thiophene*.

Sulfides and disulfides are named like ethers, according to the hydrocarbon radical they contain or as substitution products (I.U.P.A.C.), for example,  $CH_3SCH_3$ , methyl sulfide (dimethyl sulfide) or methylthiomethane. The group  $RS-$  has often been called "alkylmercapto" or "arylmercapto" (both used by *Chemical Abstracts* until 1952), but *alkylthio* is now preferred. The free radicals  $RS\cdot$  are known as "thiyl radicals." Some workers, particularly the petroleum chemists, favor the application of the "oxa-aza-thia" system to all sulfur compounds, including the simple sulfides; thus a convenient name for  $CH_3SCH_2SCH_2SCH_2SCH_2SCH_3$  is 2,4,6,8,10-pentathiahendecane.

Organic sulfides, disulfides, and polysulfides have found wide application in industry. Several such compounds are employed as antioxidants, promoters, etc., in the rubber industry, while the vulcanization process leads to the formation of sulfide bonds in rubber. A variety of elastic polymers of the polysulfide type has found application as insulators and flexible paints. Sulfides of all types are used as oil additives, insecticides, and in pharmaceuticals and dyes.

## Occurrence

Sulfides and disulfides are widely distributed in nature. A variety of sulfides occurs in petroleum, from simple alkyl sulfides to complex cyclic sulfur compounds. The nature of all of these compounds has not been completely elucidated, but has become of greater concern to the petroleum industry in recent years as higher and higher sulfur-content crudes have been refined. Some crude oils contain as much as 4-5% of sulfur, most of which is present as organic sulfides. Many sulfides and disulfides of biological importance have been discovered since 1925. This field has recently been reviewed by Challenger (11). Among the sulfides occurring in biological systems, methionine,  $CH_3SCH_2CH_2CHNH_2COOH$ , an essential amino acid, allyl sulfide and

disulfide in garlic oil, allylthiopropene in onion oil, and the vitamin biotin (*q.v.*) may be mentioned. Lanthionine is an amino acid,  $S(CH_2CHNH_2COOH)_2$ , occurring in wool, hair, and the antibiotic subtilin. The disulfide bond may well prove to be one of the most important chemical structures in biological chemistry. Its occurrence in the amino acid cystine,  $(SCH_2CH(NH_2)COOH)_2$ , provides important cross-linking bonds in the fibrous proteins, and a convenient oxidation-reduction system (cystine  $\rightleftharpoons$  cysteine) in the coenzyme glutathione, found in yeast, tissues, and red blood cells. The crucial step in the quantum conversion in photosynthesis is apparently associated with a disulfide, *6,8-thioctic acid*,  $S.S.CH_2.CH_2.CHCH_2CH_2CH_2CH_2COOH$ , which is the prosthetic group of pyruvic acid oxidase (8).

### Physical Properties

Although some of the lower-molecular-weight sulfides and disulfides have unpleasant odors, these are not usually so offensive as the mercaptan odors. In general, the disulfides seem to have stronger odors, perhaps due to decomposition to mercaptans. The presence of these substances in garlic and onion oil has been mentioned. The sulfides and disulfides are insoluble in water, but soluble in organic solvents and strongly polar solvents such as sulfuric acid. The sulfides are not associated, and their boiling points increase with the molecular weight, in a manner analogous to the ether series (see Table I). The sulfur atom is almost exactly equivalent to  $-CH_2OCH_2-$  in its effect on the boiling point. For example, *n*-propyl ether boils at 91°C. and ethyl sulfide at 92°C., *n*-butyl ether boils at 142°C. and *n*-propyl sulfide at 142°C., and *n*-hexyl ether at 225°C. and pentyl sulfide at 225°C.

The C—S bond energy is approximately 72.8 kg.-cal./mole in sulfides, and that of the —S—S— bond in disulfides is 63.8 (7). The C—S bond length in organic sulfides is 1.82 Å., and the bond angle approximately 92°. The three-dimensional structure of disulfides has been reviewed by Koch (33) who gives the following values: R—S—S— angle, 90°; —S—S— distance, 1.60 Å.; azimuthal angle, 105°.

TABLE I. Boiling Points and Melting Points of Sulfides and Disulfides.

R	RSR		RSSR	
	B.p., °C.	M.p., °C.	B.p., °C.	M.p., °C.
CH <sub>3</sub>	37.3 <sup>a</sup>	-98.2 <sup>a</sup>	110 <sup>a</sup>	-84.7 <sup>a</sup>
C <sub>2</sub> H <sub>5</sub>	92.0 <sup>a</sup>	-103.9 <sup>a</sup>	154 <sup>a</sup>	-101.5 <sup>a</sup>
<i>n</i> -C <sub>3</sub> H <sub>7</sub>	142.8 <sup>a</sup>	-102.6 <sup>a</sup>	195 <sup>a</sup>	-85.6 <sup>a</sup>
<i>n</i> -C <sub>4</sub> H <sub>9</sub>	182	—	102-102.4 <sub>10</sub>	—
<i>n</i> -C <sub>5</sub> H <sub>11</sub>	225	—	128-130 <sub>12</sub>	—
<i>n</i> -C <sub>5</sub> H <sub>11</sub>	270	—	—	—
<i>n</i> -C <sub>16</sub> H <sub>33</sub>	—	57-58 <sup>b</sup>	—	54-55.5 <sup>b</sup>
C <sub>6</sub> H <sub>6</sub>	296	-40	310	61

<sup>a</sup> Data from McAllan *et al.* (37).

<sup>b</sup> Data from Baer and Carmack (3).

**Absorption Spectra.** Simple organic sulfides exhibit a characteristic absorption maximum at about 210 mμ, while similar disulfides have one at about 250 mμ. However, these compounds differ from their oxygen analogs in that bathochromic shifts and additional maxima are observed in the presence of unsaturation in the α,β- and β,γ-positions. These differences are interpreted in terms of conjugation and hyper-



conjugation between C—S and C=C groups. Fehnel and Carmack (19) have shown similar conjugative effects between two sulfide groups or between a sulfide group and a carbonyl or aromatic group, as shown by absorption spectra. Such conjugative effects, which do not appear among the oxygen analogs, can occur in the organic sulfur compounds because of the ability of the sulfur atom to expand its valence shell.

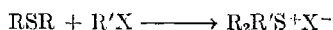
Therefore resonance,  $\text{—S—}\overset{\curvearrowright}{\text{C}}=\text{C} \longleftrightarrow \text{—}\overset{-}{\text{S}}=\overset{+}{\text{C}}\text{—C}$ , and hyperconjugation,  $\text{—S—}\overset{-}{\text{CH}_2}\text{C}=\text{C} \longleftrightarrow \text{—}\overset{-}{\text{S}}=\overset{+}{\text{CH}}\text{C}=\text{C}$ , contribute to the absorption spectra and the reactive states of the molecule. These effects are discussed in detail by Koch (33), Carmack *et al.* (3,19), and Price and Morita (43).

**Thermochromism of Disulfides.** Aryl disulfides exhibit thermochromic properties both in the dry state and in solvents (41). This was originally observed by Lecher (34) in 1915, who pointed out that phenyl disulfide was a colorless solid which formed a bright yellow melt, and that in inert solvents the color increased with increasing temperature. Schonberg has attributed this color change in disulfides to a dissociation to free thiyl radicals,  $\text{RSSR} \rightleftharpoons 2\text{RS}\cdot$ , and has also pointed out (48) that the complicated reactions that occur when aryl disulfides are maintained at high temperatures (250–300°C.) for several hours indicate stabilization of the free thiyl radicals by disproportionation.

## Chemical Reactions

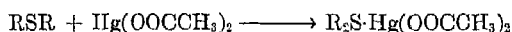
### SULFIDES

**Addition.** The sulfur atom in sulfides acts as an electron donor in many reactions to form stable ionic sulfonium salts:



This reaction occurs readily with reactive halogen compounds, such as alkyl and allyl halides, and with other alkylating agents, such as the alkyl sulfates, but the triaryl-sulfonium salts must be prepared in other ways (58). The solubility of sulfides in strong acids is undoubtedly due to the formation of sulfonium salts. Indeed, Szmant and Brost (52) have shown that in the absence of sulfonation or oxidation, aromatic sulfides dissolve in 100% sulfuric acid to produce the highly colored sulfonium ion,  $\text{Ar}_2\text{SH}^+$ , which is more stable than the corresponding oxonium salt because of resonance possibilities involving the expanded valence shell on sulfur.

Sulfides form addition compounds with salts of heavy metals such as platinum, palladium, and mercury:



These compounds are usually solids, more soluble in water than in organic solvents, and therefore aqueous mercuric chloride or mercuric acetate may be used to extract sulfides from petroleum (4). The sulfides may be recovered by treatment of the addition product with hydrogen sulfide. Sulfides have been identified by the solid products formed with palladous chloride (26–28). Certain addition reactions also involve oxidation of the sulfur.

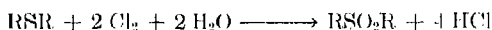
**Oxidation.** Sulfides may be readily oxidized to sulfoxides (*q.v.*) and sulfones (*q.v.*) by many of the common oxidizing agents, such as hydrogen peroxide, nitric acid, potassium permanganate, halogens or peroxybenzoic acid. A convenient procedure

utilizes 30% hydrogen peroxide in glacial acetic acid or acetone, and may lead to either the sulfoxide or sulfone, depending on concentration, time, and temperature. Recently, Djerassi and Engle (16) have found that ruthenium tetroxide has advantages in oxidizing sulfides to sulfones at low temperatures.

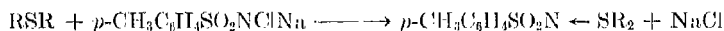
Halogens react with sulfides under anhydrous conditions to form the dihalide addition products, which are sufficiently stable to be used in the quantitative estimate of sulfide. It has been suggested that these are sulfonium salts, but they are readily hydrolyzed to sulfoxides (*q.v.*) in the presence of water:



The halogens are convenient oxidizing agents for the sulfides, yielding sulfones (*q.v.*) as final products in the presence of water. The reaction may be carried out in chloroform, acetic acid, or ether to which the stoichiometric amount of water has been added:

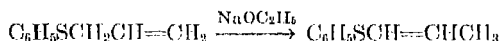


Sulfides react with the oxidizing agent chloramine-T to form stable crystalline adducts called sulfinines (sulfilimines):

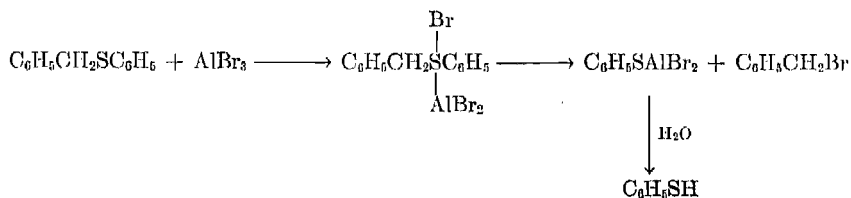


These have proved useful in the purification of liquid sulfides (38) and in the preparation of derivatives (19). See also *Sulfur compounds, organic*.

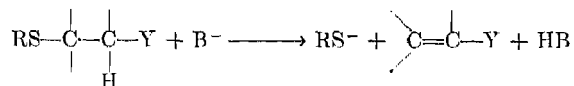
**Reactions of Active Methylene Hydrogens.** Conjugative effects of the sulfur atom due to an expanded valence shell, which were suggested by the absorption spectra, are observed in the behavior of sulfides, such as the reactivity of vinyl sulfides in copolymerization (44). This concept also explains the greater acidity of the  $\alpha$ -hydrogens in  $-\text{CH}_2\text{S}-$  compounds than in the analogous  $-\text{CH}_2\text{O}-$  compounds. For example, *n*-butyllithium metallates anisole,  $\text{C}_6\text{H}_5\text{OCH}_3$ , in the para position and thioanisole,  $\text{C}_6\text{H}_5\text{SCH}_3$ , on the methyl group. Allylthiobenzene is readily isomerized to propenylthiobenzene in the presence of alkali, while the corresponding oxygen compounds are unaffected by this treatment:



**Cleavage.** An excellent comprehensive review of this field has been made by Tarbell and Harnish (53). C—S—C bonds are cleaved much more slowly than C—O—C bonds by acidic reagents; 30% hydrogen bromide in glacial acetic acid, which is an efficient hydrolyzing agent for ethers, gave only 30% of benzyl bromide and phenyl thioacetate after refluxing for 24 hours with benzylthiobenzene. Other acidic reagents, such as hydrogen iodide, acetyl bromide, aluminum chloride, and phosphorus oxychloride behaved similarly, but aluminum bromide in chlorobenzene smoothly cleaved benzylthiobenzene in 95% yield in three hours at room temperature, to form benzyl bromide and thiophenol after the addition of water. The reaction was prevented by the presence of water, ether, nitrobenzene, or other oxygen compounds that could coordinate with aluminum bromide, indicating that a complex is intermediate in the reaction:



Although simple sulfides are stable in alkaline solution, certain unsaturated sulfides are cleaved by strong bases. As a generalization, it may be stated that a sulfide bond  $\beta$  to an unsaturated group, Y, which has an  $\alpha$ -hydrogen, will be cleaved by a base, B $^-$ , to form a mercaptide and an  $\alpha,\beta$ -unsaturated compound:



Y may be carboxyl, carbonyl, cyano, sulfonyl, or a similar unsaturated group. An example of this reaction is found in the alkaline hydrolysis of the ester ethyl  $\beta$ -phenylthiohydrocinnamate, in aqueous alcohol, to yield thiophenol and cinnamic acid:

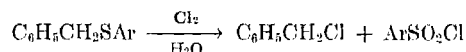


Alkaline fission may occur in more complex ways when unusual steric or electronic effects are present in the molecule (27,28,29).

Simple alkyl sulfides are cleaved quantitatively by cyanogen bromide (Von Braun method) to yield the thiocyanate and bromide, respectively:



The cleavage may take two courses with unsymmetrical sulfides to yield mixtures, but all methyl sulfides yield methyl bromide. A similar reaction occurs with certain methylene sulfides and chlorine, or even sulfonyl chloride. Aromatic benzylthio derivatives are cleaved by chlorine in the presence of water to yield benzyl chloride and the arylsulfonyl chloride:

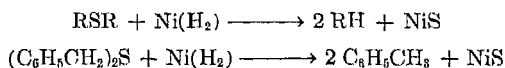


In certain cases, the reaction can be accomplished in the absence of water, and the aromatic sulfenyl halide is isolated:



indicating that this reaction is probably similar to the Von Braun reaction, with oxidation of the sulfenyl halide by chlorine and water occurring as a second step.

Although it has been known for many years that organic sulfides will react with active metal surfaces to form metal sulfides, thus accounting for the corrosive properties of these substances, their poisoning effect on catalysts, and also in some respects their value as oil additives, it has only been recently that the organic fragments produced in this reaction have been much studied. The reaction may occur with copper, lead, iron, bismuth, and other metals, but the system which has been most widely studied involves Raney nickel. Pyrophoric Raney nickel contains adsorbed hydrogen, and the reaction of sulfides with this metal is therefore a reductive desulfurization. For example, benzyl sulfide when refluxed with excess nickel in alcohol gave a nearly quantitative yield of toluene:

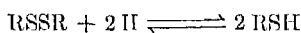


The reaction is convenient since the nickel sulfide may be filtered from the medium to leave the organic residues. It has been widely used for structure proof among organic sulfur compounds (40), and has been developed into a synthetic method for reduction of carbonyls via the mercaptals (59), etc.

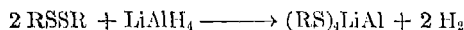
A convenient procedure for the reduction of sulfides and related compounds containing an acidic group has been developed by Schwenk *et al.* (50) which involves treating an aqueous alkaline solution of the acidic substance with a nickel-aluminum alloy. In this way the active nickel is formed directly in the reaction. *o*-Methylthiobenzoic acid was converted to benzoic acid in 75% yield by this procedure. As has been pointed out by Hurd and Rudner (25), the results obtained by desulfurization with active nickel must be interpreted with caution in structure-proof work, since nickel may cleave other types of bonds as well as carbon—sulfur bonds, and does not always cleave carbon—sulfur bonds completely.

#### DISULFIDES

**Reduction.** Disulfides are mild oxidizing agents, and as such are readily reduced to mercaptans (*q.v.*). The redox system shown by:



is an important one in biochemical systems. It has been postulated that certain antibiotics function by interfering with this system in bacterial metabolism, and the poisonous effects of arsenic and heavy metals (lewisite, mercury, lead, etc.) are also probably due to interference with this system. Reduction of the disulfide by chemical reducing agents is readily brought about under a variety of conditions, such as zinc in acetic acid and sodium in alcohol. With lithium aluminum hydride, hydrogen is liberated in stoichiometric proportion, and may be used as a quantitative estimate of disulfide in the presence of sulfide (2):

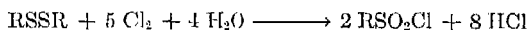
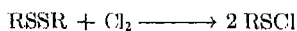


The disulfides are sufficiently strong oxidizing agents to dehydrogenate some cyclic hydrocarbons; 1,2,3,4-tetrahydronaphthalene, for example, when heated with amyl disulfide was converted to naphthalene in high yield (47). Mercaptans are oxidized by disulfides, thus effecting an exchange reaction to form mixed disulfides or disulfides corresponding to the mercaptans:

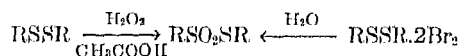


One of the most powerful reducing agents in this respect is thioglycolic acid (*q.v.*), which is used as a softener for hair because of its effect on the cross-linking disulfide bonds of cystine.

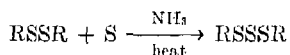
**Oxidation.** Under anhydrous conditions, disulfides are oxidized by chlorine or bromine to form the sulfonyl halides; in the presence of moisture, the oxidation is complete to the sulfonyl halide stage:



Aqueous oxidizing solutions convert the disulfides to sulfonic acids (*q.v.*). Under carefully controlled conditions, thioisulfonic esters are sometimes formed with hydrogen peroxide:

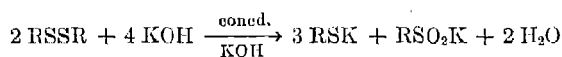


Disulfoxides of the formula  $\text{RSOSOR}$  are unknown, and all efforts to synthesize these compounds lead to the thiolsulfonic esters. For example, bromine or iodine may form the tetrahalide addition product with certain disulfides, and this might be expected to yield the disulfoxide on hydrolysis, but instead gives the thiolsulfonic ester. Disulfides are oxidized by sulfur to trisulfides, a reaction which is apparently catalyzed by ammonia:

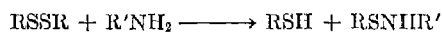


**Pyrolysis.** Alkyl disulfides decompose around  $500^\circ\text{C}$ . in the absence of oxygen to yield mercaptans, hydrogen sulfide, sulfides, and thiophenes. Phenyl disulfide, when heated at  $288^\circ\text{C}$ . for six hours in the absence of solvent or oxygen, was converted nearly quantitatively to thiophenol and thianthrene (49). This reaction may represent a disproportionation of free thiyl radicals. Benzyl disulfide when similarly treated at  $270^\circ\text{C}$ . is primarily converted to stilbene,  $\text{C}_6\text{H}_5\text{CH}:\text{CHC}_6\text{H}_5$ , hydrogen sulfide, and sulfur, but these react further to produce toluene, tetraphenylbutane, tetraphenylthiophene, etc.

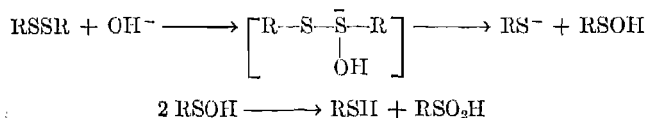
**Hydrolytic Cleavage.** Disulfides undergo a number of cleavage reactions which are most readily explained by polar attack on the  $-\text{S}-\text{S}-$  bond. For example, in strong alkali, disulfides are split to form mercaptides and sulfates:



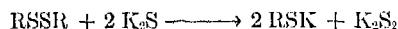
a reaction which, when followed by the characteristic nitroprosside test for mercaptide, may be diagnostic for the disulfide link. Certain polar disulfides react with ammonia or amines to give mercaptans and sulfenamides:



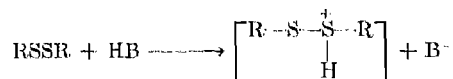
These reactions probably involve a nucleophilic attack on sulfur, with an expanded valence shell in the transition state. With hydroxide ion, the reaction is as follows:



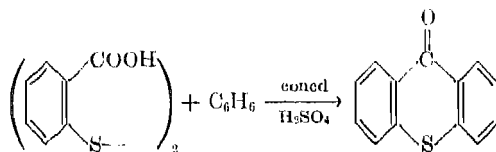
The known disproportionation of sulfenic acids explains the formation of sulfinate. Disulfides are readily cleaved by aqueous potassium sulfide to form potassium mercaptide and disulfide in a similar reaction:



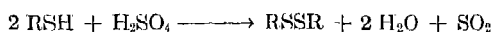
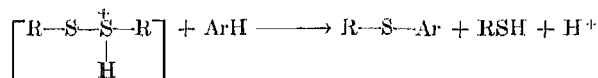
**Acid-Catalyzed Reactions.** Disulfides also undergo a series of reactions which apparently involve a sulfonium ion type of intermediate:



The intermediate then reacts further with nucleophilic reagents to form mercaptans and sulfides or related compounds. The best example of this reaction is the *Smiles reaction* of dithiosalicic acid with aromatic compounds in sulfuric acid to form thiaxanthenes:

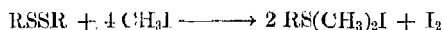


This reaction has recently been shown by Archer and Suter (1) to involve initial attack of the sulfonium ion, formed in 100% sulfuric acid, on the aromatic compound to form the sulfide and mercaptan. The sulfide then undergoes ring closure, while the mercaptan is oxidized by sulfuric acid to disulfide again:

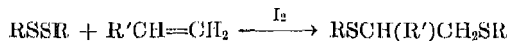


Phenyl disulfide forms thianthrene when allowed to stand in concentrated sulfuric acid. Since this reaction is promoted by electron-releasing groups on the aromatic rings, it undoubtedly falls in this category also.

Disulfides form dimethylsulfonium iodides and free iodine when refluxed with methyl iodide:



In the presence of iodine and other catalysts disulfides add to olefins (23):

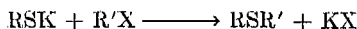


This reaction is catalyzed by boron trifluoride or *p*-toluenesulfonic acid (66).

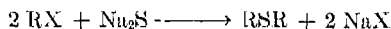
## Preparation

### SULFIDES

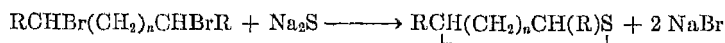
**Alkylation.** The most general reaction for the preparation of simple sulfides is the alkylation of mercaptans (*q.v.*):



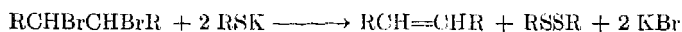
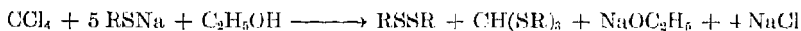
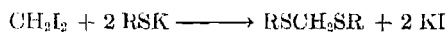
Alkyl halides, sulfates, or sulfonates have been used with mercaptides in alcohol solution. Alcohols may alkylate mercaptans under acidic conditions. Aromatic sulfides may be obtained by using aromatic thiols or active aromatic halides such as *p*-nitrochlorobenzene or *o*-chlorobenzoic acid. It is also possible to prepare both simple and mixed sulfides using two moles of the alkylating agent with a mole of sodium or potassium sulfide (17,37):



Cyclic sulfides may also be prepared by this reaction using dihalides and metal sulfides (20,57):



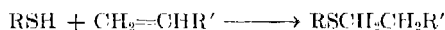
Di- and polyhalides may be used to form compounds containing more than one sulfide linkage, but since the mercaptide ion is a reducing agent, sometimes disulfides are also formed:



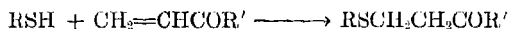
Lead mercaptides react with aryl bromides to form alkylthioaromatics in poor yield:



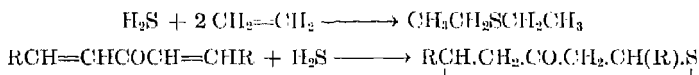
**Addition to Unsaturated Groups.** Mercaptans add to unsaturated groups to produce sulfides. The addition of mercaptans to olefins has been studied extensively, both as a synthetic method and because it is apparently involved in the rubber vulcanization process. The reaction has been briefly reviewed by Cuneen (14), and may be free-radical or polar. With impure mercaptans containing disulfides, the addition is opposite to the Markovnikov rule, and this mode of addition also occurs with pure mercaptans when catalyzed by peroxides or ultraviolet light:



With pure mercaptans, however, the reaction gives the Markovnikov product,  $\text{CH}_3\text{-CH}(\text{SR})\text{R}'$ . Some thiols add spontaneously (thioglycolic acid), while with others a catalyst must be used. Catalysts for this reaction are usually acidic, and have been the subject of many patents; for example, hydrofluoric acid (64), selenium (63), and aluminum oxide (60). The reaction proceeds more readily with  $\alpha,\beta$ -unsaturated carbonyl compounds to form the  $\beta$ -sulfides in all cases:



Alkaline catalysts have been most effective here, such as sodium ethoxide, potassium hydroxide, piperidine, or pyridine. A mixture of Triton B (benzyltrimethylammonium hydroxide) and piperidine has recently been used with considerable success. Hydrogen sulfide may add to olefins to form sulfides. This reaction has been utilized in the synthesis of cyclic sulfides (22):



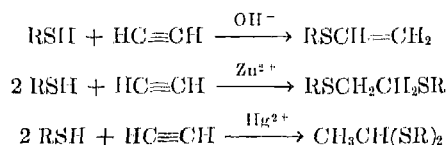
The reaction of mercaptans with olefins has been used in addition polymerization to form polyalkylene sulfides with rubber-like properties. Marvel and his co-workers (36) have shown that 1,6-hexanedithiol adds to nonconjugated diolefins (such as biallyl,  $\text{CH}_2\text{:CHCH}_2\text{CH}_2\text{CH:CH}_2$ ) under activation by ultraviolet light by a free-radical reaction to produce linear non-Markovnikov addition products. In soap emulsions, using peroxydisulfate as initiator, polymers in the molecular weight range of 25,000-60,000 have been obtained. Butadiene does not form a polymer under these conditions. The preparation and properties of polymers of the above type have been comprehensively reviewed by Marvel (35).

The comparatively little work which has been done on the addition of mercaptans to acetylenes indicates that under ordinary conditions, one mole of mercaptan adds to form the  $\alpha,\beta$ -unsaturated sulfide. Ethynyl ketones and carboxylic acids give good yields of the unsaturated  $\beta$ -sulfides using alkaline catalysts:

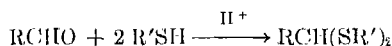


Reppe (46) reports that thiols react smoothly and practically quantitatively with acetylene in the liquid or vapor state using alkaline catalysts to form vinyl sulfides. When

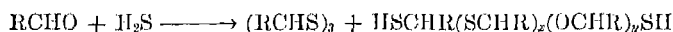
zinc or cadmium salts were used as catalysts 1,2-dithioethers were formed, while with mercuric salts and salts of some other heavy metals of the first period, 1,1-dithioethers (thioacetals or mercaptals (*q.v.*)) were obtained:



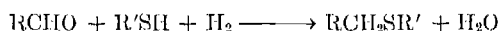
Mercaptans add to aldehydes and ketones in the presence of acid catalysts to form thioacetals:



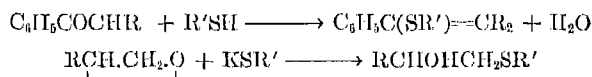
With hydrogen sulfide and acid catalysts, aldehydes and some ketones react to form cyclic trisulfides (trithianes) and/or linear polymers (9):



Simple sulfides can be prepared from the reaction of mercaptans with aldehydes under reducing conditions. Thus in the presence of cobalt polysulfide and 2,500 lb. hydrogen pressure for three hours at 175° C., aldehydes and mercaptans form sulfides (61):

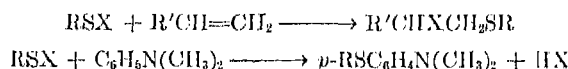


Some hindered ketones form vinyl sulfides with mercaptans (10), and mercaptides react with reactive heterocycles such as ethylene oxide, ethylenimine, or ethylene sulfide to form the hydroxy sulfide.



**Miscellaneous Methods.** Aromatic sulfides may be synthesized by reaction of the mercaptides with diazonium salts (39), but the reaction is very unsatisfactory, giving 25–30% yields at best, with disulfides formed as by-product. Sulfones can be reduced with difficulty to sulfides, using hydrogenation catalysts at high pressures and temperatures (65). Most sulfones may be reduced with lithium aluminum hydride (5) to yield sulfides, but the yields vary markedly with the nature of the sulfone. For example, ethyl sulfone was not reduced in ether in 12 hours, while thiacyclopentane dioxide gave a 75% yield of thiacyclopentane in one-half hour under identical conditions.

Sulfonyl halides add to olefins, and also substitute with reactive aromatic compounds like dimethylaniline, resorcinol, and the like, to produce sulfides (31):



Sulfur chloride and sulfur dichloride add to olefins to produce  $\beta$ -chloro sulfides (see *Gas warfare agents*).

Sulfides are formed when sulfur reacts with olefins. The reaction has been studied extensively, since it occurs in the vulcanization process. It probably involves initial free-radical attack on allylic hydrogen atoms, followed by various complex reactions leading to sulfides, disulfides, polysulfides, cyclic sulfides, etc. The subject has been reviewed by Westlake (56) and by Farmer and Shipley (18). Craig *et al.* (13) have also carefully studied the role of sulfur in the vulcanization reaction. Sulfur can

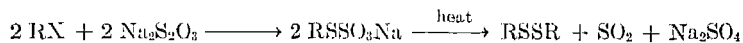


also be made to react with saturated hydrocarbons in the vapor phase over catalysts consisting of oxides or sulfides of vanadium, manganese, chromium, iron, cobalt, copper, nickel, etc., to produce various sulfur compounds, including sulfides and disulfides (62).

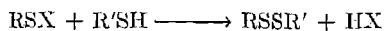
#### DISULFIDES

Although disulfides are frequently obtained as by-products in many reactions (see above), their methods of direct preparation are simple and few. The most common method is the mild oxidation of mercaptans. Such reagents as iodine, hydrogen peroxide, potassium peroxydisulfate, and even copper sulfate have been used. The reaction is more rapid in alkaline solution, and mercaptides are oxidized by air. For complex high-molecular-weight mercaptans, benzoyl peroxide in benzene is effective.

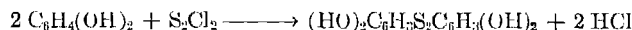
A second useful method involves the alkylation of sodium or potassium disulfide, but since these salts are always contaminated with sulfides and polysulfides, the organic sulfides and polysulfides are formed as impurities:



Disulfides are obtained by boiling alkyl halides with sodium thiosulfate. The most effective way to prepare mixed disulfides is by the reaction of sulphenyl halides with mercaptans, but they can also be obtained by the exchange reaction between disulfides and mercaptans already mentioned:



Aromatic disulfides may be obtained from the reaction of reactive aromatic compounds with sulfur chloride:

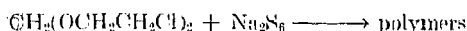


Disulfides are formed in the "doctor" treatment and several other treatments applied to petroleum products to remove mercaptans (see vol. 10, p. 143).

#### Uses

**Polymers and Polymerization.** By far the largest use of sulfides, disulfides, and polysulfides is in the polymerization industries. 2,2'-Bisbenzothiazolyl disulfide (2,2'-dithiobisbenzothiazole, Altax),  $(\text{S.C}_6\text{H}_4.\text{N:C})_2\text{S}_2$ ; tetramethylthiuram disulfide  $[\text{---} \text{C}(\text{CH}_3)_2 \text{---}]_2\text{S}_2$ ; bis(dimethylthiocarbamoyl) disulfide, TMTD, Methyl Tuads),  $[(\text{CH}_3)_2\text{NCS}]_2\text{S}_2$ ; and tetramethylthiuram monosulfide (bis(dimethylthiocarbamoyl) sulfide, TMTM Thione),  $[(\text{CH}_3)_2\text{NCS}]_2\text{S}$ , are used as accelerators for vulcanization. Phenol sulfides such as dicresol sulfides are of value as antioxidants or stabilizers for synthetic rubber latexes and coagulated polymers, and as softening agents for reclaimed vulcanizates (71). Organic tertiary disulfides are reclaiming agents for natural rubber, neoprene, and various diene elastomers (72). Alkyl polysulfides, such as *tert*-butyl trisulfide, are effective in short-stopping emulsion polymerization (70). See also *Rubber chemicals*.

Condensation polymers of the Thiokol type (see Vol. 11, p. 842) are formed by the reaction of organic dihalides with sodium polysulfides, for example:



The polysulfide polymers have unusual properties, and have found many useful applications. For example, because of their low-temperature flexibility and resistance to oil and gasoline, they have been used as sealing compounds for fuel tanks and cabins in the aircraft industry. They have also been used to prepare flexible, resilient paint coatings which are resistant to oxygen, sunlight, organic solvents, acids, and bases, and which are not crystalline at  $-65^{\circ}\text{F}$ . Such polymers have been used to impregnate leather (thus reducing its permeability to water) in the formation of flexible molding patterns and electric cable insulators, and in rubber-metal bonding adhesives.

**Oil Additives.** A number of simple sulfides and disulfides have been found to improve the properties of fuel and lubricating oils. For instance, when 0.05–1.0% by volume of an aliphatic thioether, such as *n*-dodecylthioacetic acid, is added to gasoline there is improved motor operation under icing conditions (73). Liquid diesters of bis(hydroxyalkyl) sulfides, such as  $(\text{RCOOCH}_2\text{CH}_2\text{CH}_2)_2\text{S}$ , are good pour-point depressants with a high viscosity index, good thermal stability, and high resistance to oxidation (75). Pentaerythritol tetrathioethers have been patented as lubricating oil additives (74), and some of the more complex disulfides derived from waxy phenols and related compounds have been found to effectively reduce the coefficient of friction in extreme pressure lubricants and cutting oils (67).

**Pharmaceuticals, Insecticides, and Antifungicides.** Many sulfides and disulfides have been tested for chemotherapeutic action and several have been found effective against certain organisms, but at present few, if any, have found their way into clinical practice. Sulfur itself is of definite value in certain fungus infections, and therefore a number of polysulfides have been tried in this connection. Dithiocarbamates, thiuram sulfides, and related compounds have been found to be active in this way (32), as have certain dithiosalicyl substituted benzyldenehydrazides,  $(\text{ArCH}=\text{NNHCOC}_6\text{H}_4)_2\text{S}_2$  (30). Bradsher *et al.* (6) have shown that certain rhodanines having an alkylthioalkyl side chain are effective fungistatics, but they are not more effective than analogs containing a simple alkyl side chain of the same number of atoms. Bis(*o*-aminophenyl) disulfide has been reported to be an effective antibacterial agent *in vitro* against *Staphylococcus aureus* at dilutions of 1/1,280,000 (54), and derivatives of this same compound are effective against *Spirochaeta pallida* (42). The use of the nitrogen mustards (see Vol. 7, p. 127) in the chemotherapy of malignant tumors grew out of the observation that mustard gas and related compounds such as bis(2-chlorocyclohexyl) sulfide prevent the growth of carcinomas in mice and rats (21).

A number of sulfides containing various other functional groups have proved active in various ways. The vesicant action of bis(2-chloroethyl) sulfide is well known (see *Gas warfare agents*). Ethyl phenyl sulfide has a weak anticonvulsant action, and a number of compounds have been synthesized in which a sulfur atom has replaced a  $-\text{CH}_2-$  or  $-\text{CH}=\text{CH}-$  in a side chain or ring of a physiologically active type (24). It is not surprising that these compounds usually show the same type of activity as their analogs. The compound first known in Sweden as "Antabuse" has come into clinical practice in the treatment of alcoholism, and apparently affects the metabolism of alcohol in such a way that an accumulation of acetaldehyde in the blood poisons the patient, causing extremely unpleasant effects following the ingestion of alcohol. This drug is Disulfiram, N.N.R.,  $((\text{C}_2\text{H}_5)_2\text{NCS})_2\text{S}$ , used in the rubber industry as TETD. Compounds of this same general structure have been found to be effective as growth stimulants in rice seedlings (51), and gave very good control of "black spot" in apples, caused by *Ventura inaequalis* (55). Aromatic sulfides, such as bis(*p*-chlorophenyl) sulfide, are synergistic for nicotine insecticides (69).

**Miscellaneous Uses.** The field of organic sulfur dyes (*q.v.*) is a large area which includes some sulfides and related compounds, although the structures of many of the commercially useful dyes in this series are unknown. The dyes are prepared by fusing such compounds as diphenylamine with sulfur or polysulfides in the presence of mild oxidizing agents such as  $\text{CuSO}_4$ . The compounds obtained are complex benzothiazoles, thiazines, and thianthrenes.

Several classes of long-chain sulfides have detergent properties. For example, compounds of the class  $\text{CH}_3(\text{CH}_2)_x\text{S}(\text{CH}_2)_y\text{COOH}$  where  $x + y = 12$  have such properties (45), and products of the reaction of mercaptans with ethylene oxide, such as  $\text{C}_{12}\text{H}_{25}\text{SCH}_2\text{CH}_2(\text{OCH}_2\text{CH}_2)_{11}\text{OH}$ , have been patented as surface-active agents (68). A recent patent (76) claims that corrosive attack on metal by well fluids containing water and sulfides or carbon dioxide is prevented by the addition of the reaction product of formaldehyde and hydrogen sulfide, which probably includes sulfide polymers of the formula  $\text{HOCH}_2\text{SCH}_2\text{OCH}_2\text{SCH}_2\text{OCH}_2\text{SH}$ , etc. Thiodiethylene glycol (Kromfax solvent),  $(\text{HOCH}_2\text{CH}_2)_2\text{S}$ , is a powerful neutral solvent for dyes (see *Glycols*, vol. 7, p. 251), and some of the lower-molecular-weight sulfides and disulfides, such as ethyl disulfide, have been used as solvents and vehicles for the Thiokol polymers mentioned above.

### Bibliography

- (1) Archer, S., and Suter, C. M., *J. Am. Chem. Soc.*, **74**, 4296 (1952).
- (2) Arnold, R. C., Lien, A. P., and Alm, R. M., *J. Am. Chem. Soc.*, **72**, 731 (1950).
- (3) Baer, J. E., and Carmack, M., *J. Am. Chem. Soc.*, **71**, 1215 (1949).
- (4) Birch, S. F., and McAllan, D. T., *J. Inst. Petroleum*, **37**, 443 (1951).
- (5) Bordwell, F. G., and McKellin, W. H., *J. Am. Chem. Soc.*, **73**, 2251 (1951).
- (6) Bradsher, C. K., Brown, F. C., and Grantham, R. J., *J. Am. Chem. Soc.*, **76**, 114 (1954).
- (7) Branch, G. E. K., and Calvin, M., *Theory of Organic Chemistry*, Prentice-Hall, N.Y., 1946.
- (8) Calvin, M., and Bartrop, J. A., *J. Am. Chem. Soc.*, **74**, 6153 (1952).
- (9) Campaigne, E., *Chem. Revs.*, **39**, 1-77 (1946).
- (10) Campaigne, E., and Leal, J. R., *J. Am. Chem. Soc.*, **76**, 1272 (1954).
- (11) Challenger, F., *Endeavour*, **12**, 173-81 (1953).
- (12) Connor, R., "Organic Sulfur Compounds," in Gilman, *Organic Chemistry*, 2nd ed., Wiley, N.Y., 1943, Vol. I, pp. 853-64.
- (13) Craig, D., Juve, A. E., Davidson, W. L., Semon, W. L., and Hay, D. C., *J. Polymer Sci.*, **8**, 321-35 (1952).
- (14) Cuneen, J. I., *J. Chem. Soc.*, **1947**, 36.
- (15) Dawson, T. P., *J. Am. Chem. Soc.*, **69**, 968 (1947).
- (16) Djerassi, C., and Engle, R. R., *J. Am. Chem. Soc.*, **73**, 3838 (1953).
- (17) Drahowzal, F., and Klamann, D., *Monatsh.*, **82**, 970 (1951); *C.A.*, **46**, 8038.
- (18) Farmer, E. H., and Shipley, F. W., *J. Chem. Soc.*, **1947**, 1519-32.
- (19) Fehnel, E., and Carmack, M., *J. Am. Chem. Soc.*, **71**, 84 (1949).
- (20) Fehnel, E., and Oppenlander, G. C., *J. Am. Chem. Soc.*, **75**, 4660 (1953).
- (21) Hackmann, C., *Z. Krebsforsch.*, **56**, 91 (1948); *C.A.*, **44**, 232.
- (22) Harman, D., and Vaughn, W. E., *J. Am. Chem. Soc.*, **72**, 631 (1950).
- (23) Holmberg, B., *Arkiv. Kemi, Min. Geol.*, **B13**, No. 14, 1 (1939); *C.A.*, **34**, 2341.
- (24) Houff, W. H., and Scheutz, R. D., *J. Am. Chem. Soc.*, **75**, 6316 (1953).
- (25) Hurd, C. D., and Rudner, D., *J. Am. Chem. Soc.*, **73**, 5157 (1951).
- (26) Ipatieff, V., and Friedman, B. S., *J. Am. Chem. Soc.*, **61**, 684 (1939).
- (27) Iskander, Y., and Riad, Y., *J. Chem. Soc.*, **1951**, 2054.
- (28) Iskander, Y., and Salama, A., *J. Chem. Soc.*, **1951**, 2058.
- (29) Iskander, Y., and Tewfic, R., *J. Chem. Soc.*, **1951**, 2050.
- (30) Katz, L., Karger, L. S., Schroeder, W., and Cohen, M. S., *J. Org. Chem.*, **18**, 1380 (1953).
- (31) Kharasch, N., Potempa, S. J., and Wehrmeister, H. L., *Chem. Revs.*, **39**, 269 (1946).

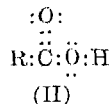
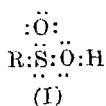
- (32) Klopping, H. L., and van der Kerk, G. J. M., *Rec. trav. chim.*, **70**, 917 (1951).
- (33) Koch, H. P., *J. Chem. Soc.*, **1949**, 387, 394.
- (34) Lecher, H., *Ber.*, **48**, 524 (1915).
- (35) Marvel, C. S., *Rec. Chem. Prog.*, **12**, 185 (1951).
- (36) Marvel, C. S., and Baumgartner, H. E., *J. Polymer Sci.*, **6**, 127 (1951).
- (37) McAllan, D. T., Cullum, T. V., Dean, R. A., and Fidler, F. A., *J. Am. Chem. Soc.*, **73**, 3627 (1951).
- (38) McCall, M. A., Tarbell, D. S., and Havill, M. A., *J. Am. Chem. Soc.*, **73**, 4476 (1951).
- (39) Miller, E., Crossley, F. S., and Moore, M. L., *J. Am. Chem. Soc.*, **64**, 2322 (1942).
- (40) Mazingo, R., Wolf, D. E., Harris, S. A., and Folkers, K., *J. Am. Chem. Soc.*, **65**, 1013 (1943).
- (41) Mustafa, A., and Kamel, M., *Science*, **118**, 411 (1953).
- (42) Pratesi, P., Raffa, L., Babaderi, B., and Nascimbene, A., *Science*, **111**, 694 (1950).
- (43) Price, C. C., and Morita, H., *J. Am. Chem. Soc.*, **75**, 4747 (1953).
- (44) Price, C. C., and Zomlefer, J., *J. Am. Chem. Soc.*, **72**, 14 (1950).
- (45) Rapoport, L., Smith, A., and Newman, M. S., *J. Am. Chem. Soc.*, **69**, 693 (1947).
- (46) Reppe, J. W., *Acetylene Chemistry*, Charles Meyer, N.Y., 1949, pp. 58-59.
- (47) Ritter, J. J., and Sharpe, E. D., *J. Am. Chem. Soc.*, **59**, 2351 (1937).
- (48) Schonberg, A., and Mustafa, A., *J. Chem. Soc.*, **1949**, 889.
- (49) Schonberg, A., Mustafa, A., and Askar, W., *Science*, **109**, 522 (1949).
- (50) Schwenk, E., Papst, D., Whitman, B., and Ginsberg, H., *J. Org. Chem.*, **9**, 1 (1944).
- (51) Scotti, T., *Notiz. malattie piante*, No. 14, **44** (1951); *C.A.*, **46**, 1694.
- (52) Szmant, H. H., and Brost, G. A., *J. Am. Chem. Soc.*, **73**, 4175 (1951).
- (53) Tarbell, D. S., and Harnish, D. P., *Chem. Revs.*, **49**, 1-90 (1951).
- (54) Tomita, M., and Watanabe, W., *J. Pharm. Soc. Japan*, **71**, 1206 (1951); *C.A.*, **46**, 7618.
- (55) Wade, G. C., *Tasmanian J. Agr.*, **22**, 293 (1951); *C.A.*, **46**, 3201.
- (56) Westlake, H. E., Jr., *Chem. Revs.*, **39**, 219 (1946).
- (57) Whitehead, E. V., Dean, R. A., and Fidler, F. A., *J. Am. Chem. Soc.*, **73**, 3632 (1951).
- (58) Wildi, B. S., Taylor, S. W., and Potratz, H. A., *J. Am. Chem. Soc.*, **73**, 1965 (1951).
- (59) Wolfrom, M. L., and Karabinos, J. V., *J. Am. Chem. Soc.*, **66**, 909 (1944).
- (60) Brit. Pat. 603,103 (June 9, 1948), B. S. Greensfelder and R. J. Moore (to Shell Development Co.).
- (61) U.S. Pat. 2,406,410 (Aug. 27, 1946), F. K. Signaigo (to Du Pont).
- (62) U.S. Pat. 2,411,236 (Nov. 19, 1946), C. M. Thacker (to Pure Oil Co.).
- (63) U.S. Pat. 2,454,108 (Nov. 16, 1948), C. T. Walling (to Du Pont).
- (64) U.S. Pat. 2,454,409 (Nov. 23, 1948), W. A. Schulze and W. W. Crouch (to Phillips Petroleum Co.).
- (65) U.S. Pat. 2,471,077 (May 24, 1949), R. L. Moore and R. A. Trimble (to Shell Development Co.).
- (66) U.S. Pat. 2,519,586 (Aug. 22, 1950), D. A. McCauley and A. P. Lien (to Standard Oil Co. of Indiana).
- (67) U.S. Pat. 2,555,370 (June 5, 1951), C. F. Prutton (to Lubrizol Corp.).
- (68) U.S. Pat. 2,565,986 (Aug. 28, 1951), J. F. Olin (to Sharples Chemical Co.).
- (69) U.S. Pat. 2,572,898 (Oct. 30, 1951), C. F. Woodward and E. T. Mayer (to U.S. of America, Secy. of Agriculture).
- (70) U.S. Pat. 2,574,020 (Nov. 6, 1951), W. W. Crouch (to Phillips Petroleum Co.).
- (71) U.S. Pat. 2,581,919 (Jan. 8, 1952), H. E. Albert (to Firestone Rubber Co.).
- (72) U.S. Pat. 2,593,279 (April 15, 1952), J. C. Elgin (to U.S. Rubber Reclaiming Corp.).
- (73) U.S. Pat. 2,600,113 (June 10, 1952), A. R. Jones and J. O. Smith (to Standard Oil Development Co.).
- (74) U.S. Pat. 2,602,050 (July 1, 1952), R. T. Sanderson (to The Texas Co.).
- (75) U.S. Pat. 2,603,604 (July 15, 1952), S. A. Ballard, R. C. Morris, and J. L. Van Winkle (to Shell Development Co.).
- (76) U.S. Pat. 2,605,223 (July 29, 1952), L. C. Case (to Gulf Oil Co.).

E. E. CAMPAIGNE

**SULFIMINES, SULFILIMINES.** See *Sulfides, organic*, p.298; *Sulfur compounds, organic*.

## SULFINIC ACIDS

Sulfinic acids,  $\text{RSO}_2\text{H}$ , are most commonly shown electronically as in formula (I). The sulfinic acids differ in structure from the carboxylic acids (II) in that there is no true double bond between sulfur and oxygen, but rather one that is intermediate between a double bond and a semipolar bond (see p. 377).



The known aliphatic sulfinic acids are not as numerous as the aromatic analogs. They are named by adding the suffix -sulfinic acid to the name of the hydrocarbon, for example,  $\text{CH}_3(\text{CH}_2)_2\text{CH}(\text{SO}_2\text{H})\text{CH}_3$  is 2-pentanesulfinic acid and  $\text{C}_6\text{H}_5\text{SO}_2\text{H}$  is benzenesulfinic acid.

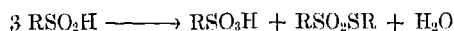
Free sulfinic acids are not known to occur naturally, and the natural occurrence of their derivatives is rare. A recently reported example is the thiosulfinic ester  $\text{CH}_2\text{:}-\text{CHCH}_2\text{S}(\rightarrow\text{O})\text{SCH}_2\text{CH:CH}_2$ , an antibacterial agent (3).

## Physical and Chemical Properties

The low-molecular-weight aliphatic sulfinic acids are viscous oils. Of the higher-molecular-weight aliphatic acids, 1-dodecanesulfinic acid has been isolated as a crystalline solid, m.p.  $29-30^\circ\text{C}$ . Aromatic sulfinic acids are more commonly obtained as crystalline solids.

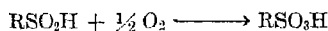
The sulfinic acids are stronger acids than the corresponding carboxylic acids and weaker acids than the corresponding sulfonic acids (*q.v.*). The ionization constants of benzenesulfinic acid and *p*-toluenesulfinic acid at  $25^\circ\text{C}$ . are approximately  $3 \times 10^{-2}$ .

The low-molecular-weight aliphatic members are readily decomposed and are therefore usually isolated as their more stable salts. The aliphatic acids tend to undergo disproportionation to sulfonic acids and thiosulfonic *S*-esters:

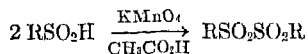


The comparatively more stable aromatic members will also decompose as above on prolonged standing.

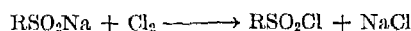
Sulfinic acids (and their salts) are readily oxidized to sulfonic acids (*q.v.*) (and their salts):



The product of another oxidation reaction may be an  $\alpha$ -disulfone:

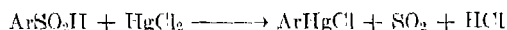


The oxidation of a sulfinic acid to a sulfonic acid proceeds slowly on exposure to air and rapidly with such agents as hydrogen peroxide, potassium permanganate, and nitric acid. With halogens and positive-halogen compounds, salts of sulfinic acids are converted to the corresponding sulfonyl halides:



The acids are subject to cleavage of the carbon-sulfur bond by strong bases and

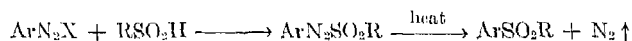
certain other vigorous reagents. Some value in obtaining organomercury compounds and in structure proofs is attached to the reaction:



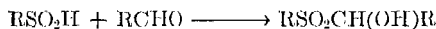
Alkylation and arylation are of particular importance in identifying sulfinic acids and in preparing sulfones (4):



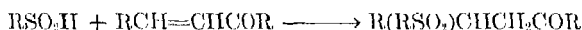
Although the nucleophilic activity of sulfonates is not as great as that of the corresponding mercaptides, this reaction proceeds satisfactorily with many alkyl halides, activated aryl halides, sulfates, and other active alkylating agents. However, positive-halogen compounds will convert the sulfinic acids to sulfonyl halides, and with *gem*-dihalides the reactions stop at the  $\alpha$ -halo sulfone. An interesting arylation is the reaction of a sulfinic acid with a diazonium salt to give a diazosulfone which may be thermally decomposed to a sulfone (*q.v.*):



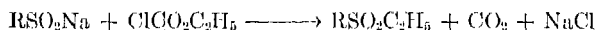
Sulfinic acids tend to parallel the reactions of bisulfites with unsaturated groups, for example, they form unstable addition compounds with aldehydes:



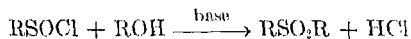
Furthermore, they add to a variety of activated olefinic bonds as in  $\alpha$ ,  $\beta$ -unsaturated ketones and esters to form the corresponding sulfones:



In the above reactions, sulfones and not sulfinic esters are formed. *Sulfinic esters* have been prepared by reaction of sulfonates with ethyl chlorocarbonate:

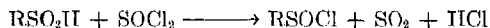


Sulfinic esters are also obtained by the action of alcoholic hydrogen chloride on the free acid. However, a more general method for preparing these compounds is to treat the corresponding sulfinyl chloride with the appropriate alcohol in the presence of a base, such as pyridine or potassium carbonate:



Since the sulfur atom in sulfinic acids and their derivatives possesses a pyramidal configuration, the esters can be resolved. (See Vol. 12, p. 861; Vol. 13, p. 378.)

*Sulfinyl chlorides* are readily obtained from sulfinic acids. A convenient reagent for this conversion is an excess of thionyl chloride in dry ether:



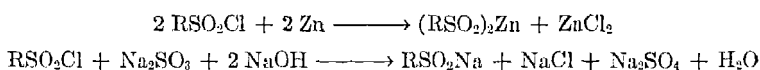
The action of ammonia or amines on sulfinyl chlorides forms *sulfinamides*,  $\text{RSONH}_2$ .

Like carboxylic acids, sulfinic acids can be dehydrated by the action of strong dehydrating agents to *sulfinic anhydrides*,  $(\text{RSO})_2\text{O}$ .

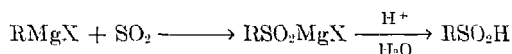
### Preparation

Sulfinic acids are frequently prepared by reducing sulfonyl chlorides. This is especially true in the aromatic series due to the availability of the starting sulfonic

acids by way of sulfonation reactions. Two commonly employed reducing agents are zinc dust and alkali sulfites:

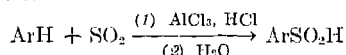


Another general preparative procedure for sulfinic acids involves the reaction of aliphatic and aromatic organometallic compounds with sulfur dioxide. The convenient Grignard reagent has been used extensively for this purpose. A common procedure is to bubble dry sulfur dioxide through the Grignard reagent at a low temperature:

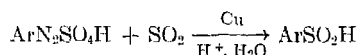


More recently, the corresponding organolithium compounds have been used to advantage.

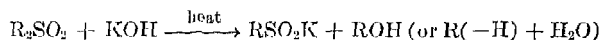
Several aromatic sulfinic acids have been prepared by a Friedel-Crafts procedure, in which sulfur dioxide is passed into a mixture of the aromatic compound, aluminum chloride, and hydrogen chloride. The solvent is generally an excess of the aromatic compound or carbon disulfide:



Aromatic sulfinic acids may also be obtained by reaction of diazonium sulfates with sulfur dioxide in the presence of copper or cuprous salts:

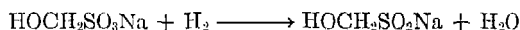


Many aliphatic and aromatic sulfinic acids may be prepared by cleaving sulfones with basic reagents:

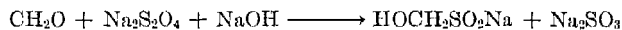


$\gamma$ -Disulfones are particularly subject to this type of reaction. A related procedure for preparing certain ortho-substituted aromatic sulfinic acids is the base-catalyzed Smiles' rearrangement of *o*-hydroxyaryl sulfones, *o*-aminoaryl sulfones, and related compounds. See p. 341.

In addition to the preceding general preparative methods, many other reactions leading to sulfinic acids have been described in the literature (5). One of these is the reduction of sodium formaldehyde bisulfite to the industrially important sodium formaldehydesulfoxylate:



In a related process, formaldehyde and sodium dithionite are the reactants:



Although the salt formed is now considered to be derived from the sulfinic acid form ( $\text{HSO}_2\text{H}$ ) rather than the dihydroxy form ( $\text{S(OH)}_2$ ) of sulfoxylic acid, it is still named as a sulfoxylate(2). See *Sulfur compounds, inorganic*, p. 418.

### Bibliography

- (1) Connor, R., "Organic Sulfur Compounds," in Gilman, *Organic Chemistry*, Vol. I, Wiley, N.Y., 1943.

- (2) Goehring, M., *Naturwissenschaften*, **32**, 42 (1944); Faessler, A., and Goehring, M., *ibid*, **39**, 169 (1952).  
 (3) Small, L. D., Bailey, J. H., and Cavallito, C. J., *J. Am. Chem. Soc.*, **69**, 1710 (1947).  
 (4) Suter, C. M., *Organic Chemistry of Sulfur*, Wiley, N.Y., 1944, p. 667.  
 (5) Truce, W. E., and Murphy, A. M., *Chem. Revs.*, **48**, 69 (1951).

W. E. TRUCE

**SULFISOXAZOLE**,  $C_{11}H_{13}N_3O_3S$ . See *Sulfa drugs*.

**SULFITE PROCESS**. See *Pulp*, Vol. **11**, p. 254.

**SULFITES**. See such articles as *Barium compounds*; *Calcium compounds*. See also *Sulfuric and sulfurous esters*.

**SULFITE WASTE LIQUOR**. See *Alcohol, industrial*, Vol. **1**, p. 274; *Pulp*, Vol. **11**, p. 261; *Vanillin*.

**SULFOALKYLATION**. See *Sulfonation and sulfation*.

**SULFOCHLORINATION**. See *Sulfonation and sulfation*.

**SULFO-J ACID**,  $H_2N(HO)C_{10}H_4(SO_3H)_2$ . See *Amino naphthols and amino naphtholsulfonic acids*, Vol. **1**, p. 737.

## SULFONAMIDES

Sulfonamides have the general formula  $RSO_2NR'R''$ , where R is an organic radical, and R' and R'' are hydrogen or organic radicals. This designation has also been used loosely as a general name for sulfanilamide derivatives following the discovery of the chemotherapeutic activity of these compounds. See *Sulfa drugs*.

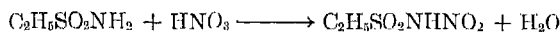
Some representative sulfonamides are listed in Table I.

### Aliphatic Sulfonamides

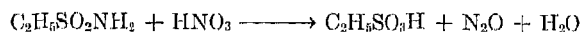
**Physical and Chemical Properties.** The aliphatic sulfonamides are, in general, colorless solids.

Although the alkanesulfonamides are relatively stable, cleavage of methanesulfonanilides has been carried out using hydrobromic acid and phenol as in the case of aromatic sulfonamides (23,25) (see p. 314).

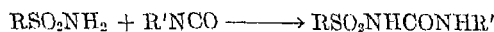
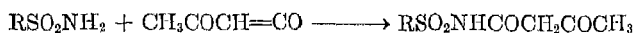
At a low temperature, nitric acid forms the nitramide:



while at a higher temperature, the reaction takes place explosively (24):



The unsubstituted sulfonamides are readily acylated with diketene to acetoacetyl derivatives, and with isocyanate to the substituted ureas (24):



With aromatic diazonium salts, the following reaction takes place (24):

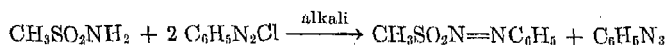




TABLE I. Sulfonamides.

Name	Formula	M.p., °C.	References
Methanesulfonamide	$\text{CH}_3\text{SO}_2\text{NH}_2$	84-85	6
Ethanesulfonamide	$\text{C}_2\text{H}_5\text{SO}_2\text{NH}_2$	58	12
1-Propanesulfonamide	$\text{CH}_3\text{CH}_2\text{CH}_2\text{SO}_2\text{NH}_2$	52	5
1-Butanesulfonamide	$\text{CH}_3(\text{CH}_2)_3\text{SO}_2\text{NH}_2$	45	5
1,3-Propanedisulfonamide	$\text{CH}_2(\text{CH}_2\text{SO}_2\text{NH}_2)_2$	169, 172.5- 174.5	4,7
1,4-Butanedisulfonamide	$(-\text{CH}_2\text{CH}_2\text{SO}_2\text{NH}_2)_2$	179.5-180.5, 182, 183	1a, 7, 8
Ethylenesulfonamide	$\text{CH}_2=\text{CHSO}_2\text{NH}_2$	87	4
$\alpha$ -Toluenesulfonamide	$\text{C}_6\text{H}_4\text{CH}_2\text{SO}_2\text{NH}_2$	104-105	13
Phenethylsulfonamide	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{SO}_2\text{NH}_2$	121.5-122.5	14
Benzenesulfonamide	$\text{C}_6\text{H}_5\text{SO}_2\text{NH}_2$	153	24
<i>o</i> -Toluenesulfonamide	$\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{NH}_2$	156	24
<i>p</i> -Toluenesulfonamide	$\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{NH}_2$	137	24
1-Naphthalenesulfonamide	$\text{C}_{10}\text{H}_7\text{SO}_2\text{NH}_2$	150	24
2-Naphthalenesulfonamide	$\text{C}_{10}\text{H}_7\text{SO}_2\text{NH}_2$	212	24
3-Pyridinesulfonamide	$\text{C}_5\text{H}_4\text{NSO}_2\text{NH}_2$	110-111	24
6-Quinolinesulfonamide	$\text{C}_9\text{H}_6\text{NSO}_2\text{NH}_2$	191-192	3
2-Imidazolesulfonamide	$\text{HN}.\text{CH}:\text{CH}.\text{N}:\text{CSO}_2\text{NH}_2$	236-236.5	22
2-Benzimidazolesulfonamide	$\text{HN}.\text{C}_6\text{H}_4.\text{N}:\text{CSO}_2\text{NH}_2$	214	22
1,2,4-Triazole-3-sulfonamide	$\text{HN}.\text{CH}:\text{N}.\text{N}:\text{CSO}_2\text{NH}_2$	224-225.5	22, 32
2-Thiazolesulfonamide	$\text{S}.\text{CH}:\text{CH}.\text{N}:\text{CSO}_2\text{NH}_2$	120.5-121	22
2-Benzothiazolesulfonamide	$\text{S}.\text{C}_6\text{H}_4.\text{N}:\text{CSO}_2\text{NH}_2$	177	22
2-Pyrimidinesulfonamide	$\text{N}:\text{CH}.\text{CH}:\text{CH}.\text{N}:\text{CSO}_2\text{NH}_2$	180.5-181	22
2-Pyrazinesulfonamide	$\text{CH}:\text{N}.\text{CH}:\text{CH}.\text{N}:\text{CSO}_2\text{NH}_2$	166-166.5	22

**Preparation.** The alkanesulfonamides are prepared by the reaction of the appropriate alkanesulfonyl chloride with ammonia or amines (24):



In certain special cases, the reaction between a sulfonyl fluoride and urea at higher temperatures is used (29).

**Uses.** These compounds have not found extensive commercial use, probably because of their cost, but 1-propanesulfonamide and 1-butanedisulfonamide are described as selective solvents for isolation of saturated or unsaturated hydrocarbons from mixtures of these hydrocarbons (26).

The sulfonamides obtained by the reaction of methanesulfonyl chloride (17) or  $\alpha$ -toluenesulfonyl chloride (16) with various amines have been used as a means of identification of those amines. The reaction products of methanesulfonyl chloride with amino acids have been used in a similar fashion (24).

Various aldehyde and ketone condensation compounds are claimed as resinous products (24). See also *Amino resins and plastics*.

The *N*-dichloro derivatives, prepared by treatment of the sulfonamide with alkali and chlorine (19,27), are said to be effective germicides (19).

The compound  $C_6H_4CH_2SO_2NHC_6H_4COOH$  (30), carinimide, has been used with various drugs to delay excretion so that smaller doses of the drugs may be used.

The tripropyllead derivatives of alkanesulfonamides are potent sterminators (18).

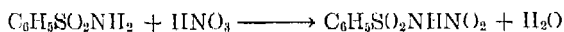
### Aromatic Sulfonamides

**Physical and Chemical Properties.** The aromatic sulfonamides are usually colorless, crystalline solids only slightly soluble in cold water. The aromatic sulfonamides are reported to be associated in benzene and other organic solvents, but probably not in polar solvents (24). The simple monosubstituted sulfonamides are soluble in aqueous alkali.

Although the aromatic sulfonamides are quite stable to alkali except on fusion, when their behavior is like that of aromatic sulfonic acids (*q.v.*), they may be cleaved by heating with strong hydrochloric or sulfuric acid (24). The drastic conditions for this procedure, however, limit its usefulness where recovery of the amine is desired. The use of a mixture of hydrobromic acid and phenol at reflux temperatures (23) or of hydrobromic acid, phenol, and acetic acid at lower temperatures (25) gives better results in many cases. The hydrobromic acid-phenol process is not a simple hydrolysis since an oxidation-reduction reaction involving the sulfur-containing fragments and the hydrobromic acid is involved. The phenol serves as a bromine acceptor to protect other components, as well as being a solvent. Sulfonamides have also been cleaved in acetic acid and hydrochloric acid with the aid of zinc chloride or by heating with aqueous pyridine hydrochloride (15). With anhydrous pyridine hydrochloride, the following rearrangement takes place (15):

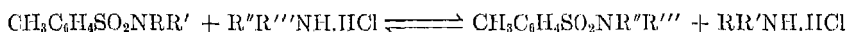


With 100% nitric acid in sulfuric acid, sulfonamides are converted to nitramides (24):

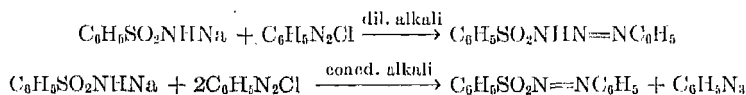


Benzenesulfonamide reacts with nitrous acid to give benzenesulfonic acid and *N,N*-bis(phenylsulfonyl)hydroxylamine (24),  $(C_6H_5SO_2)_2NOH$ .

Transamidation of sulfonamides takes place on heating with amine hydrochlorides (15):

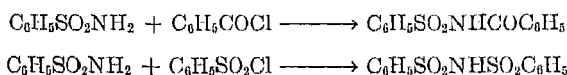


Aromatic sulfonamides condense with aromatic diazonium salts to give one of two types of products, depending upon the concentration of alkali used (24):

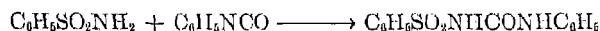


The simple aromatic sulfonamides such as benzenesulfonamide and toluenesulfonamide react readily with aldehydes and ketones.

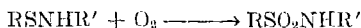
The carboxyl or sulfonyl halides react with aromatic sulfonamides (24):



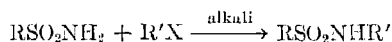
Acylation takes place also with isocyanates (21,24):



**Preparation.** The aromatic sulfonamides are prepared by the reaction of an aromatic sulfonyl chloride with ammonia or the desired amine (24). In special cases, the heating of the ammonium salt of an aromatic sulfonic acid leads to formation of the aromatic sulfonamide, but this procedure is much less effective than in the case of the carboxamides (24). Another process involves the reaction of a sulfinic acid, ammonia, and chlorine (2). The oxidation of sulfenamides to sulfonamides has been used in preparing sulfanilamide derivatives (see *Sulfa drugs*):



In the preparation of substituted sulfonamides from simple sulfonamides, alkylations may be carried out by treatment with alkyl halides, alkyl sulfates, or active aryl halides in the presence of alkali (24):



**Uses.** The solubility of simple sulfonamides in alkali is useful in the isolation and identification of primary, secondary, and tertiary amines by the Hinsberg procedure (Vol. 1, p. 708) with some exceptions (24). The sulfonamide derivatives of various alkyl- (9), chloro- (10), or alkoxy- (11) substituted aromatic hydrocarbons serve to identify the parent compounds. The *N*-halogen-substituted compounds such as chloramine T, N.F. IX (the sodium derivative of *N*-chlorotoluenesulfonamide) (24), from the reaction of sulfonamides with halogen or hypochlorous acid, are used as sources of active chlorine for sterilizing and bleaching. (See also *Antiseptics*, Vol. 2, p. 82; *Chloramines*, Vol. 3, p. 670.) *o*-Sulfobenzoic imide,  $\text{C}_6\text{H}_4\text{SO}_2\text{NH.CO}$ , is the

well-known sweetening agent (*q.v.*) saccharin. The compound *p*-(di-*n*-propylsulfamoyl)-benzoic acid (probenecid, N.N.R., Benemid),  $\text{HOOC.C}_6\text{H}_4\text{SO}_2\text{N}(\text{CH}_2\text{CH}_2\text{CH}_3)_2$ , is also used for delaying excretion of drugs (33). The *m*-nitrobenzenesulfonamides are used in the treatment of coccidiosis in chickens (31). *N*-(*p*-Nitrophenyl)-3,4-dichlorobenzenesulfonamide and related compounds are described as insecticides (28). The tripropyllead derivatives of aromatic as well as aliphatic sulfonamides are potent sternutators (18). The reaction products of sulfonamides with aldehydes or ketones are claimed to be useful as plasticizers, resins, and waxes (1,24). (See also *Amino resins and plastics*.) Organotin aromatic sulfonamide derivatives are used as stabilizers for vinyl halide resins (34).

### Heterocyclic Sulfonamides

Although pyridinesulfonamides (24) have been described, until recently relatively few other heterocyclic sulfonamides were known. In connection with a study of the inhibition of carbonic anhydrases (20,22), several heterocyclic sulfonamides were prepared by the reaction of heterocyclic sulfonyl chlorides with ammonia. The heterocyclic rings involved included imidazole, triazole, tetrazole, thiazole, thiadiazole, pyrimidine, and pyrazine (22,32).

The most active carbonic anhydrase inhibitor *in vitro* is benzothiazole-2-sulfonamide (20). 2-Acetylamino-1,3,4-thiadiazole-5-sulfonamide (Diamox) was most effective *in vivo* and is now used clinically as a diuretic, especially in congestive heart failure (20,22,32):

## Bibliography

- (1) Asinger, F., Elbender, F., and Böck, E., *Ber.*, **B75**, 42-48 (1942).
- (1a) Aelony, D., *Ind. Eng. Chem.*, **46**, 587 (1954).
- (2) Carter, P. R., and Hey, D. H., *J. Chem. Soc.*, **1948**, 147-49.
- (3) Chelintsev, G. V., and Zakotin, V. N., *J. Gen. Chem. (U.S.S.R.)*, **11**, 729-30 (1941); *C.A.*, **36**, 477 (1942).
- (4) Clutterbuck, P. W., and Cohen, J. B., *J. Chem. Soc.*, **121**, 120-28 (1922).
- (5) Duguet, M., *Bull. acad. roy. Belg.*, **1902**, 79-94; *Chem. Zentr.*, **1902**, 855.
- (6) Dutt, P. K., *J. Chem. Soc.*, **125**, 1463-65 (1924).
- (7) Griffin, J. W., and Hey, D. H., *J. Chem. Soc.*, **1952**, 3334-40.
- (8) Helferich, B., and Grünert, H., *Ber.*, **B74**, 1531-32 (1941).
- (9) Huntress, E. H., and Autenrieth, J. S., *J. Am. Chem. Soc.*, **63**, 3446-48 (1941).
- (10) Huntress, E. H., and Carten, F. H., *J. Am. Chem. Soc.*, **62**, 511-14 (1940).
- (11) Huntress, E. H., and Carten, F. H., *J. Am. Chem. Soc.*, **62**, 603-04 (1940).
- (12) James, J. W., *J. prakt. Chem.*, **26**, 378-84 (1882).
- (13) Johnson, T. B., and Ambler, J. A., *J. Am. Chem. Soc.*, **36**, 372-85 (1914).
- (14) Johnson, T. B., and Sprague, J. M., *J. Am. Chem. Soc.*, **58**, 1348-52 (1936).
- (15) Klamann, D., and Hofbauer, G., *Ann.*, **581**, 182-97 (1953).
- (16) Marvel, C. S., and Gillespie, H. B., *J. Am. Chem. Soc.*, **48**, 2943-44 (1926).
- (17) Marvel, C. S., Helfrick, M. D., and Belsley, J. P., *J. Am. Chem. Soc.*, **51**, 1272-74 (1929).
- (18) McCombie, H., and Saunders, B. C., *Nature*, **159**, 491-94 (1947).
- (19) Mel'nikov, N. N., Sukhareva, N. D., and Kavenoki, F. Y., *J. Applied Chem. (U.S.S.R.)*, **18**, 568-70 (1945); *C.A.*, **40**, 5696 (1946).
- (20) Miller, W. H., Dessert, A. M., and Rohlin, R. O., Jr., *J. Am. Chem. Soc.*, **72**, 4893-96 (1950).
- (21) Petersen, S., *Ber.*, **83**, 551-58 (1950).
- (22) Rohlin, R. O., Jr., and Clapp, J. W., *J. Am. Chem. Soc.*, **72**, 4890-92 (1950).
- (23) Snyder, H. R., and Heckert, R. A., *J. Am. Chem. Soc.*, **74**, 2006-09 (1952).
- (24) Suter, C. M., *The Organic Chemistry of Sulfur*, Wiley, N.Y., 1944, ch. VI.
- (25) Weisblat, D. I., Magerlein, B. J., and Meyers, D. R., *J. Am. Chem. Soc.*, **75**, 3630-32 (1953).
- (26) U.S. Pat. 2,385,981 (Oct. 2, 1945), B. S. Friedman (to Universal Oil Products Co.).
- (27) U.S. Pat. 2,394,902 (Feb. 12, 1946), M. Engelmann (to Du Pont).
- (28) U.S. Pat. 2,435,274 (Feb. 3, 1948), W. F. Hester (to Rohm & Haas Co.).
- (29) U.S. Pat. 2,450,863 (Oct. 5, 1948), M. S. Altamura (to Socony-Vacuum Oil Co.).
- (30) U.S. Pat. 2,531,367 (Nov. 21, 1950), J. M. Sprague (to Sharp and Dohme, Inc.).
- (31) U.S. Pat. 2,531,755 (Nov. 28, 1950), E. Waletzky (to American Cyanamid Co.).
- (32) U.S. Pat. 2,554,816 (May 29, 1951), J. W. Clapp and R. O. Rohlin, Jr. (to American Cyanamid Co.).
- (33) U.S. Pat. 2,608,506 (Aug. 26, 1952), J. M. Sprague and C. S. Miller (to Sharp and Dohme, Inc.).
- (34) U.S. Pat. 2,634,281 (April 7, 1953), G. P. Muck and E. Parker (to Advance Solvents & Chemical Corp.).

M. E. HULTQUIST

**SULFONATED ACIDS, ALCOHOLS, OILS, etc.** See *Sulfonation and sulfation*;  
*Surface-active agents*.

## SULFONATION AND SULFATION

The term *sulfonation* designates any procedure by which the sulfo group,  $\text{—SO}_2\text{OH}$ , or the corresponding salt or sulfonyl halide is attached to a carbon atom, or sometimes a nitrogen atom. Included are those methods in which the sulfur at a lower state of valence is already attached to the carbon, the sulfonation process in these cases comprising oxidation. Methods of attaching the  $\text{—SO}_2\text{OH}$  group to nitrogen are usually designated *N-sulfonation*, or *sulfamation* after the products commonly so formed. The term sulfonation is also loosely used to designate treatment of any organic compound with sulfuric acid regardless of the nature of the products formed.

Specialized types of sulfonation include *sulfochlorination*, introduction of an  $\text{—SO}_2\text{Cl}$  group into an alkane using sulfuryl chloride or sulfur dioxide with chlorine; *chlorosulfonation*, introduction of an  $\text{—SO}_2\text{Cl}$  group into an aromatic or heterocyclic compound with chlorosulfonic acid; *sulfoxidation*, direct sulfonation of an alkane with sulfur dioxide and oxygen; and *sulfoalkylation*, attachment of a sulfoalkyl group to an organic compound.

*Sulfation* designates the establishment of an  $\text{—OSO}_2\text{OH}$  grouping on carbon.

Important general reference works on these subjects include those of Suter (31), covering the literature through 1941, generally on the preparation and properties of organic sulfates and sulfonic acids; Suter and Weston (33), specifically on the direct sulfonation of aromatic hydrocarbons and their halogen derivatives as of 1946; and Groggins (18), from the unit process standpoint with special emphasis on physicochemical and thermodynamic factors. Sulfonation and sulfation have been reviewed annually in some detail since 1941 in *Industrial and Engineering Chemistry*, the same general scheme as that employed here being used.

### Sulfonation

Sulfonates may be differentiated into four main chemical types: aliphatic and alicyclic (p.323), aromatic (p. 326), heterocyclic (p.329), and *N-sulfonates* (333). The first three categories are similar in having the  $\text{—SO}_2\text{OH}$  group attached to a carbon atom, the nature of which alone determines the classification. Thus, alkanesulfonic acids may also contain aromatic or heterocyclic groupings, for example, 1-phenyl-1-propanesulfonic acid,  $\text{C}_6\text{H}_5\text{CH}(\text{C}_2\text{H}_5)\text{SO}_2\text{OH}$ .

Three additional types of sulfonates, derived from petroleum fractions (p. 330), from lignin (p. 332), and from fatty oils (p. 332), are important commercially. They are made by largely empirical procedures, are indeterminate in composition, and may comprise mixtures of one or more of the four chemical types of sulfonates together with sulfates and other sulfur compounds.

Most uses for sulfonates depend upon the presence in the molecule of the hydrophilic, highly polar  $\text{—SO}_2\text{OH}$  group. In detergents, and similarly in wetting, emulsifying, and dispersing agents, the water-soluble sulfonate grouping is combined with an oil-soluble organic portion in many possible ways to yield a variety of desired effects. For dyes, mothproofing compounds, and synthetic tanning agents it serves to attach the organic molecule firmly to the fiber or leather. Ion-exchange resins function as strong acids with complete water insolubility, an unusual combination of properties leading to many applications. On the other hand, water-soluble sulfonated resins and polymers are of interest as synthetic gums and thickening agents.

Sulfonates are also used as intermediates for the preparation of other chemicals

by replacement of the sulfonate grouping, especially phenols by caustic fusion. Phenol, resorcinol, the naphthols, various hydroxyanthraquinones, and 8-hydroxyquinoline are notable examples of products made thus from the corresponding sulfonates.

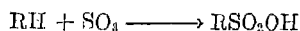
Sulfonyl chlorides,  $\text{RSO}_2\text{Cl}$ , are of special interest as providing a simple route to sulfonate derivatives such as amides, esters, and mercaptans. Alkanesulfonyl chlorides are employed as tanning agents or used to make detergents and elastomers, while the aromatic analogs yield sulfa drugs and insecticides. See also such articles as *Detergency*; *Emulsions*; *Ion exchange*; *Phenol and phenols*; *Sulfa drugs*; *Sulfonic acids*; *Surface-active agents*.

The principal sulfonation procedures may be classified as follows: (1) direct treatment with sulfur trioxide or a compound thereof; (2) oxidative procedures; (3) sulfite reactions; and (4) condensation and polymerization methods. The broad classifications direct and indirect are sometimes used to indicate whether any sulfonation procedure involves one or more steps.

**(1) Direct Treatment with Sulfur Trioxide or a Compound Thereof.** This procedure, by far the most widely applicable, is used for the preparation of the four chemical types of sulfonates, as well as for the treatment of fatty oils and of petroleum fractions. It will be referred to here as *direct sulfonation*.

Concentrated sulfuric acid and oleums of various strengths are the most common reagents for direct sulfonation. The physical properties of the system  $\text{SO}_3\text{-H}_2\text{O}$  have been reviewed from the standpoint of sulfonation (18). Other reagents finding extensive use include sulfur trioxide itself, various addition compounds of sulfur trioxide with organic compounds such as dioxane or pyridine, and chlorosulfonic acid. Also of this type, but less often applied are fluosulfonic acid, acid sulfates, pyrosulfates, and aminosulfonic (sulfamic) acid.

Sulfur trioxide (see *Sulfuric acid*) is theoretically the most efficient and direct sulfonating agent of this type since only direct addition is involved according to the equation:



On the other hand, use of any of the compounds of sulfur trioxide is always complicated by concomitant liberation of the respective compounding reagent (for example, water, hydrogen chloride, or pyridine), which renders such reagents less efficient than sulfur trioxide, although they have other advantages. Sulfuric acid and free sulfur trioxide have opposite properties as sulfonating agents as summarized in Table I for the case of aromatic hydrocarbons. Oleum (a solution of sulfur trioxide in 100% sulfuric

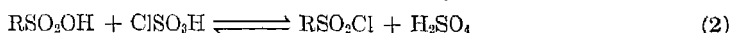
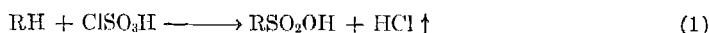
TABLE I. Comparison of Sulfuric Acid and Sulfur Trioxide as Sulfonating Agents.

Factor	$\text{H}_2\text{SO}_4$	$\text{SO}_3$
Reaction rate	Slow	Instantaneous
Heat of reaction	Requires heat for completion	Strongly exothermic throughout
Extent of reaction	Partial	Complete
Availability	Universal	Recent*
Spent acid	Usually substantial	None
By-product formation	Slight	Extensive in some cases
Reactor capacity	Substantial	Minimum
Viscosity of reaction mixture	Low	High in some cases

\* Liquid form commercially available in the U.S. since 1947; previously available as converter gas or by distillation from oleum.

acid, see *Sulfuric acid*) has often proved a practical compromise between these two extremes. The advantages of sulfur trioxide, and correspondingly of oleums, as noted in Table I (rapid and complete reaction, minimum reactor capacity, and absence of spent acid) have become increasingly attractive industrially because of higher labor and fixed capital costs and the necessity to obviate waste acid disposal, whereas the disadvantages (high heat of reaction leading to darkening or decomposition, and high viscosity) can often be overcome by engineering design, choice of conditions, or use of a solvent. A trend has in fact been noted toward the use of stronger sulfonating agents of this type.

Chlorosulfonic acid (*q.v.*) is used almost entirely for the preparation of aromatic or heterocyclic sulfonyl chlorides by the following reaction sequence:

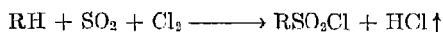


Reaction (1) is sometimes used to prepare sulfonic acids, in spite of the fact that the evolution of *HCl* and the inevitable partial occurrence of reaction (2) are objectionable.

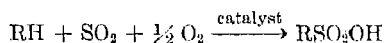
Sulfuric acid, oleum, and chlorosulfonic acid are ordinarily used in excess, thereby incidentally functioning as cheap, low-viscosity solvents for the sulfonic acid or sulfonyl chloride formed. Sulfur trioxide may sometimes be used directly as the commercially available liquid, or it may be easily vaporized (b.p. 44.8°C.) and possibly diluted with an inert gas prior to introduction into the sulfonation vessel. Liquid sulfur dioxide is an excellent sulfonation solvent for use with sulfur trioxide, chlorosulfonic acid, or oleum. However, the problems of solvent recovery have strongly deterred its industrial acceptance. In the preparation of sulfonyl chlorides (with chlorosulfonic acid) no solvent is used in industrial practice; chloroform is often employed as the reaction medium for laboratory preparations. Sulfur trioxide can advantageously be used with various chlorinated solvents with which it is miscible, such as tetrachloroethylene, carbon tetrachloride, or trichlorofluoromethane.

The reactivity of sulfur trioxide may be varied by the formation of a suitable complex or addition compound. Thus, the pyridine complex,  $\text{C}_5\text{H}_5\text{N} \cdot \text{SO}_3$ , one of the least reactive, does not sulfonate benzene or its homologs; the thioxane adduct yields naphthalene-1-sulfonic acid, but not disulfonic acids, nor does it react with benzene under the same conditions, whereas the dioxane compound will sulfonate both benzene and naphthalene.

**(2) Oxidative Procedures.** Commercial development of this approach is relatively recent and is especially applicable for preparing alkanesulfonates. One such procedure, known as *sulfochlorination*, involves direct treatment of alkanes with a mixture of sulfur dioxide and chlorine in the presence of light or other catalysts to form the sulfonyl chlorides as follows:



Sulfonyl chloride,  $\text{SO}_2\text{Cl}_2$ , reacts similarly. The closely related procedure of *sulfoxidation* proceeds by the overall reaction:



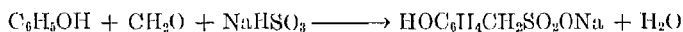
The oxidation of thiols (mercaptans) and of thiol derivatives is often used to prepare sulfonates of the aliphatic and heterocyclic series. Various oxidizing agents may be used, the reaction being expressed as follows:



The corresponding sulfonyl chloride is formed when aqueous chlorine is used as the oxidizing agent, as follows:



**(3) Sulfite Reactions.** Sulfite reactions are used considerably for the preparation of aliphatic sulfonates, and to a lesser degree for the preparation of aromatic compounds. Metallic sulfites are the most common reagents, although sulfurous acid (sulfur dioxide and water) is sometimes employed. Alkenes, alkylene oxides, aldehydes, and ketones add bisulfites to yield alkanesulfonates in the first case and hydroxyalkanesulfonates in the other three cases. Formaldehyde-sodium bisulfite reacts with active hydrogen in various compounds to introduce the  $-\text{CH}_2\text{SO}_2\text{ONa}$  group by *sulfomethylation*, as follows for the cases of phenol and an amine:



These reactions have had considerable industrial application in the preparation of a variety of products.

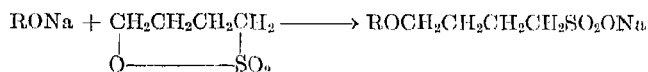
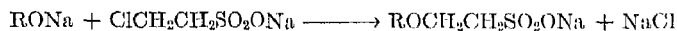
The reaction of an alkyl halide with sodium sulfite (the *Strecker reaction*) has proved a useful tool in the laboratory and to some extent industrially:



This reaction can be used under more drastic conditions to prepare sulfonates in the benzene and anthraquinone series.

**(4) Condensation and Polymerization Methods.** This classification involves the preparation of complex sulfonates from simpler ones, either by polymerization of an unsaturated sulfonate or, more frequently, by condensation with other organic compounds.

*Sulfoalkylation* is a condensation-type reaction which has been studied extensively using as sulfoalkylating agents the salts of *N*-methyltaurine,  $\text{CH}_3\text{NHCH}_2\text{CH}_2\text{SO}_3\text{H}$ , 2-hydroxyethanesulfonic acid (isethionic acid), 2-chloroethanesulfonic acid, or aliphatic sultones, such as those from hydroxypropane- or -butanesulfonic acid. These compounds have been reacted with such diverse materials as long-chain acid chlorides, phenols, thiophenols, amines, alcohols, starch, and cellulose (14). Examples of this type of reaction with sodium 2-chloroethanesulfonate and the sultone from 4-hydroxybutanesulfonic acid follow:



The similar reaction sulfomethylation is considered under "Sulfite Reactions."

Condensation of formaldehyde with phenolic sulfonic acids or with naphthalene-sulfonic acids yields resins with varying degrees of solubility in water depending upon the conditions. The reactions involved are the standard ones of phenol-formaldehyde resin formation. These products are manufactured as tanning or dispersing agents and as ion-exchange resins.

**Industrial Equipment and Operation.** Most industrial sulfonations are conducted on a batch scale and basically comprise simple mixing of a liquid sulfonating agent



with the organic compound in a reaction kettle of standard design. Jackets or coils are usually necessary to provide heating or cooling, and efficient agitation is required to facilitate heat transfer, especially since many sulfonation reaction mixtures are viscous. These considerations apply generally to all four types of sulfonation procedures but are notably not true of sulfochlorination or sulfoxidation, which require special apparatus.

A typical batch reactor for direct sulfonation consists of a kettle (18) equipped with a jacket and an efficient agitator, both of which are essential since many sulfonic acids have high viscosity and heat must usually be applied or removed during reaction. The order of mixing the reagents may be the addition of the organic compound to the sulfonating agent (as for anthraquinone, and in all chlorosulfonations), the reverse procedure (as for "dodecylbenzene," see p. 327), or the incremental addition of either or both reagents (as in preparing 1,5-naphthalenedisulfonic acid). Special ball mill sulfonators, equipped for operation under vacuum, are used for solid or extremely viscous sulfonations (18). This type of apparatus is commonly employed in the baking process for sulfonating aromatic amines. When sulfur trioxide is used as the sulfonating agent, it is often introduced as a gas diluted with air.

Continuous direct sulfonation is used for a few products processed in large quantities. This approach has been considered for dodecylbenzene, petroleum oils, and fatty oils. The monosulfonation of benzene, a step in the manufacture of phenol, is conducted continuously by the Tyrer process.

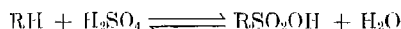
Specialized equipment is employed for sulfochlorination (22) since this reaction is catalyzed by light. Steel towers, plastic-coated to resist the corrosive action of hydrogen chloride, are suitable. Illumination is provided by mercury vapor lamps inserted in transverse quartz tubes located in the lower section of the tower. The reaction may be run batchwise or continuously. Similar apparatus is used for sulfoxidation. However, for the aqueous oxidative chlorination of bis(*o*-nitrophenyl) disulfide to the sulfonyl chloride, only a standard lead-lined kettle is required.

Sulfite reactions (sulfomethylation, addition to ethylene oxide, the Strecker reaction, addition to maleic acid esters) are conducted in standard reaction kettles using an aqueous or aqueous-alcoholic solution of sodium sulfite or bisulfite. The Strecker reaction and addition to maleic esters are run in lead-lined reactors under slight pressure (about 2 atm.) at about 100°C., while a brick-lined vat is suitable for sulfomethylation. A higher temperature (145–150°C.) and pressure (4–5 atm.) is required to replace aromatic chlorine, as in the preparation of *o*-sulfobenzoic acid,  $\text{HOCC}_6\text{H}_4\text{SO}_2\text{OH}$ .

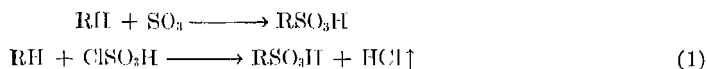
Standard equipment is likewise suitable for condensation reactions in both the aliphatic and the aromatic series. Many of these condensations, including the preparation of ion-exchange resins, tanning agents, and the surface-active agent Igepon T, are conducted in aqueous solutions at temperatures ranging from room temperature up to about 100°C. The sulfoethylation of methylamine with sodium chloroethanesulfonate is carried out at 85°C. under pressure in an iron reactor. In the preparation of Igepon A, a viscous liquid mixture of solid sodium isethionate and oleoyl chloride is heated and agitated in a lead-lined, heavy-duty mixer. The product is first converted to a crumbly solid, then to waxy flakes which comprise the final product.

**Physicochemical and Kinetic Factors in Aromatic Sulfonation.** Since the sulfonation of aromatic compounds in general, especially hydrocarbons, is of paramount interest, both industrially and for laboratory preparation, consideration has been given

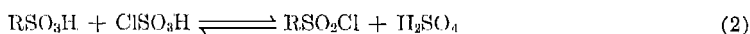
to the more fundamental aspects of this reaction. A predominant characteristic of the aromatic sulfonation reaction is its reversibility in the presence of water:



This means that, if sulfuric acid is used, water must be removed to complete sulfonation. This is usually accomplished in practice by physical methods. Anhydrous sulfonations go to completion:



The chlorosulfonation of aromatic compounds to yield sulfonyl chlorides is a two-step process of which reaction (1) above is the first step and the second step, reaction (2), is:



It is an equilibrium reaction which may be taken toward completion by the use of excess chlorosulfonic acid, chemical removal of sulfuric acid as formed, or physical removal of the organic sulfonyl chloride.

The position taken by a sulfonate group entering an aromatic hydrocarbon is strongly influenced by temperature. This fact, when considered in the light of the reversible nature of the reaction, means that the isomers obtained will depend not upon which ring position is most easily sulfonated, but upon which isomer is most stable at the temperature used, provided sufficient time is allowed to achieve equilibrium.

The process of steaming a sulfonic acid to recover the aromatic compound by reversal of the sulfonation reaction, known as *hydrolytic desulfonation*, is a useful technique in its own right especially in the case of hydrocarbon sulfonates. Since each hydrocarbon has a characteristically different desulfonation temperature, this approach can be used to separate isomers. In the manufacture of naphthalene-2-sulfonic acid, the 15% content of undesired 1-sulfonate is removed by steaming; the 2-isomer is stable. This reaction is also undoubtedly involved in the recovery of refinery acid sludges by steaming, and it has been adopted for the recovery of chlorobenzene from the corresponding sulfonic acid produced as a by-product during the manufacture of the insecticide DDT. The desulfonation reaction has proved an indispensable tool in studying the chemical structure of sulfonated petroleum fractions.

Ease of sulfonation of hydrocarbons increases with increasing methylation of the benzene ring, and with an increase in the number of rings. Isomers vary in this respect, a determining factor being the tendency of an entering sulfonate group to avoid a position adjacent to another group. Polycyclic ring systems, such as anthracene or phenanthrene, sulfonate so easily that polysulfonates are formed even under such mild conditions that some of the hydrocarbon remains unsulfonated. For this reason, such sulfonations have been studied very little. Introduction of a hydroxyl group into a hydrocarbon generally facilitates sulfonation, whereas sulfonation is rendered more difficult by presence of halogen, nitro, or carboxyl groups.

The major side reactions noted in the sulfonation of aromatic compounds are: sulfone formation, polysulfonation, oxidation, de-alkylation, and rearrangement. The last three side reactions often occur together, especially during the Jacobsen rearrangement of tetra- and pentaalkylated benzene hydrocarbons.

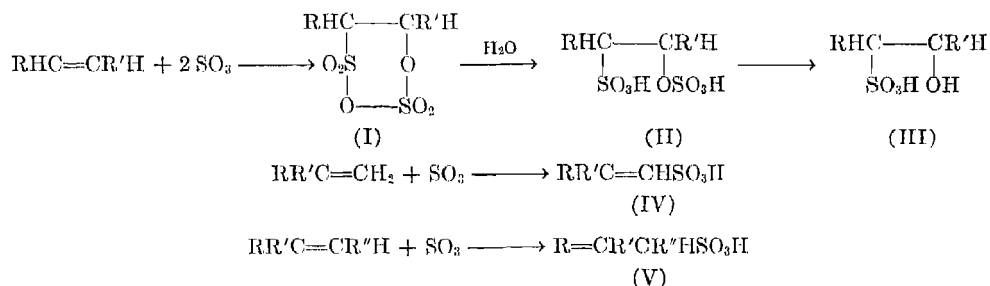
Kinetic studies of the sulfonation reaction have been rendered difficult by several unfavorable factors, including the extreme rapidity of the reaction when sulfur trioxide is used and its extreme slowness during the final stages when sulfuric acid is used. Two reaction mechanisms appear possible with sulfuric acid, one involving the ions  $\text{SO}_3\text{H}^+$  and  $\text{HSO}_4^-$ , the other involving molecular  $\text{SO}_3$  and  $\text{H}_2\text{SO}_4$ . The second appears preferable, although there is probably no physical distinction between the two in aqueous sulfuric acid (2).

#### ALIPHATIC AND ALICYCLIC (CYCLOALIPHATIC) SULFONATES

Commercial development of these sulfonates is comparatively recent since it is dependent upon the availability of newly accessible raw materials, such as methane-thiol (methyl mercaptan) or polyethylene, or novel processes of sulfonation, for example, sulfochlorination.

**Direct Sulfonation.** Alkanes and cycloalkanes react only with strong reagents (oleum or sulfur trioxide), and then primarily when oxidation is the initial step. The oxidation products, apparently largely comprising the corresponding alkenes and cycloalkenes, are not isolated as such, but undergo immediate sulfonation, among other reactions, to yield complex mixtures (30). Consequently, this approach is not suitable for preparative purposes. It occurs as an undesirable side reaction during the sulfonation of petroleum fractions.

Alkenes and cycloalkenes, on the other hand, react easily with oleum or sulfur trioxide to yield one or more of several possible products according to the scheme:



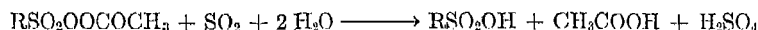
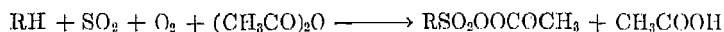
In the last equation, R must have a hydrogen atom that can migrate, leaving the bivalent radical represented by  $\text{R}=\text{}$ . (Sulfuric acid, however, yields sulfates, the formation of which is discussed separately under "Sulfation.") The substituted "carbyl sulfate" (I) may sometimes be isolated as such, or as its partial or complete hydrolysis products (II) and (III). Which of these types of products will be obtained in any case will depend upon the organic compound used as well as upon the sulfonating agent and the conditions of sulfonation and aftertreatment. Noteworthy studies of this reaction include the work of Suter and co-workers (32) on the preparation of long-chain hydroxy sulfonates (structure III) using dioxane- $\text{SO}_3$ , and that of Terent'ev and others (14) who sulfonated a series of alkadienes to products of types (IV) and (V) with pyridine- $\text{SO}_3$ . Experimental sulfonation of rubber with oleum to yield ion-exchange resins presumably involves similar reactions. A variation of this procedure, involving treatment of an alkene (hexadecene) with acetyl sulfate (acetic anhydride-sulfuric acid) has been used commercially in Germany to produce the hydroxy sulfonate of type (III) marketed as Amphoseife 18. The hydroxyl is acetylated, but removal of the acetyl group as acetic acid is accomplished by steaming. Alkenes

react with chlorosulfonic acid to yield the corresponding substituted 2-chloroethanesulfonic acids only when diethyl ether is used as solvent. Significantly, with no solvent or with other solvents, no sulfonic acid is formed, the chlorosulfonic acid organic ester being obtained instead by sulfation. Acetylene reacts with four moles of sulfur trioxide, forming a product of type (I), which upon hydrolysis yields acetaldehyde-disulfonic acid in its hydrated or dihydroxy form,  $(\text{HO})_2\text{CHCH}(\text{SO}_3\text{H})_2$ , a compound of structure (III). This acid has been used experimentally as a source of the sulfoethylidene group,  $=\text{CHCH}_2\text{SO}_3\text{Na}$ , for preparing ion-exchange resins and other sulfonates.

Aliphatic aldehydes and ketones are easily sulfonated with dioxane- $\text{SO}_3$  on the carbon adjacent to the carbonyl group (14,15). The procedure is simple, the yields are generally good, mono- or disulfonic acids may be obtained depending upon the proportions used, and the reaction is widely applicable. Likewise, saturated aliphatic acids are easily sulfonated on the C-2 with sulfur trioxide used either as liquid or as vapor (15). A technical palmitic acid-stearic acid mixture was sulfonated thus in Germany to yield the textile auxiliary Amphoseife DN. Interestingly, phenylalkanoic acids react preferentially with the aliphatic carbon rather than with the easily sulfonated phenyl group.

**Oxidative Procedures.** The sulfochlorination reaction, first patented by Reed in the U.S. in 1936, had immediate and intensive commercial development by the Du Pont company (22) and by I. G. Farbenindustrie in Germany (16) for the production of detergents at minimum cost. The organic raw materials were, respectively, a petroleum white oil and a hydrogenated gas oil obtained by the Fischer-Tropsch process. The sulfonate detergents were formed by alkaline hydrolysis of the sulfonyl chlorides obtained by the sulfochlorination reaction. Annual production of the German product Mersolate reached 80,000 tons by the end of World War II. Processing difficulties, due to the corrosive action of the hydrogen chloride formed and to the inability to carry the reaction to more than partial completion, led, however, to its virtual abandonment in the U.S. for detergent production, and even in Germany the commercial future of this process appears in doubt. Interest still continues for the preparation of the sulfonyl chloride tanning agents (Immergans). Another promising special application of sulfochlorination involves the conversion of polyethylene to an elastomer which can be cured with various inorganic or organic agents to a synthetic rubber of outstanding abrasion resistance and durability on exposure to oxygen, ozone, heat, and weather. Chemically, the elastomer is a high-molecular-weight, chlorinated, polysulfonyl chloride. The sulfochlorination reaction has been used experimentally to introduce the  $-\text{SO}_2\text{Cl}$  group into alkanes that also contain other groups such as phenyl, ester, or hydroxyl.

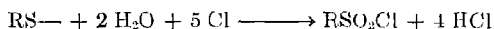
The sulfoxidation reaction was developed in Germany, in preference to sulfochlorination, for detergent manufacture since the use of chlorine and the formation of corrosive hydrogen chloride are not involved, even though in its preferred form the reaction yielded both acetic and sulfuric acids as by-products:



The practical and theoretical aspects of this procedure have been reviewed (14). Other compounds (for example, ethers, ketones, carboxylic acids, esters, chlorides,

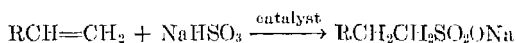
anhydrides, and nitriles) can also be sulfonated by sulfoxidation. Apparently this reaction has not yet seen extensive commercial application.

The oxidation of thiols (mercaptans, thiophenols, etc.) and of thiol derivatives (disulfides, thiosulfates, isothiuronium salts, etc.) is a widely applicable approach for the preparation both of sulfonic acids and of sulfonyl chlorides. The lower alkane-sulfonic acids are so produced commercially, possibly by oxidation with air in the presence of a catalytic quantity of nitrogen oxides. Nitric acid oxidation of aliphatic disulfides has also given good results. Chlorination of the thiol or the thiosulfate in aqueous acetic acid is a favored laboratory procedure for preparing aliphatic, alicyclic, and aromatic-aliphatic sulfonyl chlorides (15) by the general reaction:



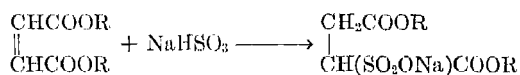
The sulfonyl chlorides are convenient intermediates for the preparation of various sulfonate derivatives such as the esters and amides.

**Sulfite Reactions.** The direct addition of bisulfites to alkenes in the presence of peroxide catalysts has been established as a general reaction by Kharasch and co-workers (22):



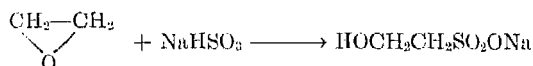
This reaction has been studied industrially (16) for the possible production of detergents from long-chain 1-olefins of petroleum origin.

Heteroconjugate systems (conjugate systems involving non-carbon atoms as well as carbon atoms) add bisulfites with ease, no catalyst being required. This reaction is applied commercially to prepare wetting agents (Aerosols, Dismulgan VII) as follows from various long-chain esters of maleic acid (27):



A variation of this reaction involves a similar addition to compounds of the type  $\text{RCOCH=CHCOOR}'$ , where R is derived from an alkylated benzene and R' from a long-chain alcohol.

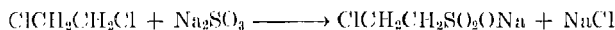
Epoxides as a class react easily with bisulfites. In the specific case of ethylene oxide:



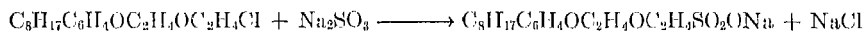
the product, sodium isethionate, is a useful building block, or sulfoalkylating agent, for the preparation of more complex sulfonates.

Sulfomethylation, introduction of the  $-\text{CH}_2\text{SO}_3\text{ONa}$  grouping using formaldehyde-sodium bisulfite, has proved a simple and mild procedure for sulfonating compounds containing active hydrogen (phenols, ketones, amines, amides, and sulfonamides) (14). The first two types of compounds sulfomethylate on carbon, the last three on nitrogen. This reaction has been applied industrially to prepare azo dyes (Ionamines) for cellulose acetate. Condensation with phenol and excess formaldehyde yields ion-exchange resins; these may be regarded as phenol-formaldehyde resins containing sulfomethyl groups. Sulfomethylation on nitrogen has been used to enhance the water solubility of pharmaceuticals, the nuclear sulfonates being in contrast less effective and more toxic (15).

The Strecker reaction, substitution of organic halogen with a sodium sulfonate grouping by reaction with sodium sulfite, has been studied extensively. It has been shown (16) to be a simple, rapid, and general procedure for preparing arylmethanesulfonates by chloromethylation of aromatic hydrocarbons. Commercially, the Strecker procedure has been employed to prepare sodium 2-chloroethanesulfonate:

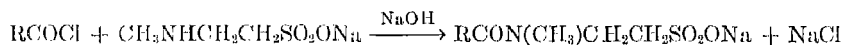


This compound is used to prepare other sulfonates by sulfoalkylation. A second commercial application is for the manufacture of surface-active agents (Tritons):



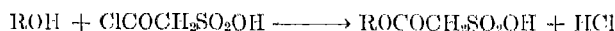
The wetting agent sodium lauryl sulfoacetate is similarly prepared from lauryl chloroacetate.

**Condensation and Polymerization Methods.** The sulfoalkylation reaction is used industrially for manufacturing the wetting agent Igepon A by heating oleic acid or its chloride with sodium isethionate, and also Igepon T by condensing oleoyl chloride with the sodium salt of *N*-methyltaurine, as follows:



Sodium 2-chloroethanesulfonate is especially convenient for sulfoethylating amines, and in fact is reacted with methylamine to yield *N*-methyltaurine by one commercial process. It has been used experimentally to sulfoethylate starch, cellulose, aromatic amines, and long-chain fatty acid amides. Sulfomethylation on nitrogen or carbon is accomplished with formaldehyde-sodium bisulfite (as discussed under "Sulfite Reactions"). Sulfomethylation on the oxygen of phenols is effected by heating their sodium salts with sodium iodomethanesulfonate in the presence of copper catalyst to form compounds of structure  $\text{ROCH}_2\text{SO}_2\text{ONa}$ .

The related reaction *sulfoacylation* has been extensively studied for rendering pharmaceuticals or dyes water-soluble. Sulfoacetyl chloride is a typical reagent:



Sulfoalkylation and sulfoacylation have been used industrially for the manufacture of azo dyes for cellulose acetate (Solacets).

The polymerization of ethylenesulfonic acid has been studied for the preparation of ion-exchange resins. Copolymers containing varying percentages of ethylenesulfonic acid, or of other monomers such as sodium allylsulfonate, (2-propene-1-sulfonate), show useful gradations in hydrophilic properties.

#### AROMATIC SULFONATES

This group comprises the most important industrial sulfonates, including detergents, tanning agents, ion-exchange resins, and intermediate sulfonates for preparing dyes, pharmaceuticals, and phenolic compounds. The hydrocarbon sulfonates are the outstanding category within this group, and direct sulfonation is by far the most useful procedure for preparing these compounds.

**Direct Sulfonations.** *Hydrocarbons.* The monosulfonation of benzene is of commercial importance as being intermediate to one process for producing phenol (*q.v.*), and to the only established process for manufacturing resorcinol (*q.v.*). Although there are several procedures for preparing benzenesulfonic acid (*q.v.*), only the Tyrer process is reported to be used in the U.S. at present. In a preferred form, this

operation comprises the liquid-phase treatment of benzene with low-strength oleum, followed by continuous removal of water at an elevated temperature (for example, 180°C.) by countercurrent treatment with benzene vapor in a multiple-unit cascade system substantially to complete the reaction of the sulfuric acid. The simplest possible preparative procedure, namely, direct reaction of benzene with sulfur trioxide, is rendered impractical by excessive by-product sulfone formation. An indirect procedure for accomplishing this without sulfone formation is the Dennis and Bull process, which, however, has to date involved too many processing difficulties to achieve commercial acceptance in spite of recent improvements.

Introduction of a second sulfonate group into the benzene ring is more difficult; one commercial process (18) involves treatment of the monosulfonic acid with oleum for several hours over the range 30–35°C. This procedure yields a large quantity of spent sulfuric acid; recent work has shown, however, that the disulfonic acid may be satisfactorily prepared by treating the monosulfonic acid with sulfur trioxide. Thus the formation of spent acid is largely eliminated.

The sulfonation of dodecylbenzene (a mixture of hydrocarbons derived from petroleum) has become very important for the large-scale manufacture of household and industrial detergents and wetting agents. Expansion has been sharp with nearly a twelvefold increase from 1943 to 1951, reaching a total of about 150,000 tons on a 100% sodium sulfonate basis. This type of sulfonation is therefore by a large margin the major one in production. The hydrocarbon, referred to commercially as "dodecylbenzene detergent alkylate," is produced cheaply from abundant petroleum raw materials (tetrapropylene or kerosene, and benzene) and is easily sulfonated to yield a detergent of good color, odor, and performance. These advantages have made a strong appeal to the numerous American manufacturers of soaps and surface-active compounds, and many of them purchase this hydrocarbon for sulfonation.

The most common reagent for this sulfonation is 20% oleum used in a batch operation (28). In outline, the process involves addition of the oleum (1.25 pounds per pound hydrocarbon) gradually to the alkylate with stirring and cooling over a period of 1–1.5 hours in the temperature range of 25–30°C., after which the mixture is digested for about 2 hours at 25°C. to complete the reaction. Water is then added to cause stratification into layers of sulfonic acid and spent sulfuric acid; the former is neutralized to the desired detergent and the latter is discarded. An alternative working-up procedure involves neutralization of the entire sulfonation mixture to yield a "low active" product containing a relatively large percentage of sodium sulfate.

Dodecylbenzene is easily sulfonated, permitting the use of 98% acid if desired. On the other hand, it is not likely to break down even when treated with as strong a reagent as sulfur trioxide vapor. Thus it becomes possible to choose any sulfonating agent in this broad concentration range. As long as this type of product was made in small quantities, a careful choice of the optimum reagent and reaction conditions was not especially critical. Recently, however, with greatly increased volume and competition, higher freight rates, stricter legislation on disposal of waste acid, demand for improved quality of product, and the trend toward a variety of formulations, it has become necessary to appraise with care the various factors inherent in the use of different reagents and processes. Dodecylbenzene differs from benzene or toluene in having a high boiling point which precludes completion of the sulfonation reaction by distillative removal of water by a Tyrer-type approach. Consequently, the large excess of acid required to complete the reaction must usually be recovered in spent form. The use of

sulfur trioxide vapor is the only practical method for avoiding the spent acid (17). Also, this reagent yields a sulfonate of 95% active ingredient content, while the standard process as detailed above gives a product of maximum 88% activity.

Another noteworthy sulfonation in the benzene hydrocarbon series is that of polystyrene. Two types of sulfonates are of interest: one, water-insoluble, produced in bead form from styrene-divinylbenzene copolymer and used as an ion-exchange resin; the other, water-soluble, produced from styrene homopolymer and employed as a synthetic gum, as a tanning agent or soil-conditioning compound. In the former case, the heterogeneous reaction is accomplished by preswelling the beads with an organic solvent and then sulfonating with excess concentrated sulfuric acid at 100°C. (35). The second sulfonation is conducted with sulfur trioxide either as a complex or in solution in a prehalogenated solvent. Other reagents give excessive cross-linking by by-product sulfone formation leading to a water-insoluble product.

Interest in the sulfonation of toluene has been stimulated by its availability in quantity from petroleum sources, combined with a shortage of cresols. A laboratory process study (12) showed a 95% total isomer yield by adding 96% sulfuric acid to the hydrocarbon as fast as compatible with control of the reaction, followed by the removal of water by distillation with excess toluene to complete the sulfonation. Lower reaction temperatures favor formation of the ortho isomer.

The naphthalenesulfonic acids (*q.v.*) are of major industrial importance as intermediates for dyes, wetting agents, and tanning agents.

*Miscellaneous Aromatic Compounds.* The sulfonation of aniline and a number of its ring-substituted derivatives is used extensively for producing dye intermediates (1). In some cases, as with *o*- or *p*-anisidine or 2,5-dichloroaniline, liquid-phase sulfonation at moderate temperatures (for example, 30–80°C.) with acid or oleum is suitable. More often, the baking process is used, notably for aniline, the toluidines, xylydines, and chlorinated anilines. In this procedure the solid sulfate, prepared as a paste by direct reaction of the amine with concentrated sulfuric acid, is baked in an oven at an elevated temperature (for example, 200–300°C.). A modified process, operating at 150–200°C., uses *o*-dichlorobenzene as an inert solvent assisting in the rapid and continuous removal of water to complete sulfonation (23). Alexander has studied the mechanism of sulfonation of aromatic amines. Direct sulfonation of 1- and 2-naphthylamines leads to several important dye intermediates (see *Naphthylamines and naphthylaminesulfonic acids*).

Anthraquinonesulfonic acids (see *Anthraquinone derivatives*) are key intermediates for the preparation of important dyes. They are produced by the sulfonation of anthraquinone with oleum.

The sulfonates of nitrobenzene, nitrotoluenes, and nitrochlorobenzenes are used as dye intermediates. The reaction is conducted at moderate temperatures using oleum (1). Violent explosions have occurred during these sulfonations.

Phenolic compounds sulfonate with ease. Thus, phenol reacts to the extent of 94% when heated with an equimolar quantity of concentrated sulfuric acid for 2 hours at 100°C. (15). The cresols react less completely, with considerable variation in the three isomers. These sulfonates find application as intermediates for preparing tanning agents and ion-exchange resins. (See *Phenolsulfonic acids*.) Chlorinated phenols are sulfonated in the preparation of dye intermediates (3). Naphtholsulfonic acids are important dye intermediates; several are made by direct sulfonation (see *Naphthols and naphtholsulfonic acids*).



**Chlorosulfonation.** The chlorosulfonation reaction is extensively employed to introduce the  $\text{—SO}_2\text{Cl}$  grouping into aromatic nuclei. The two reactions involved and the methods employed for driving the second (equilibrium) reaction toward completion were cited in a preceding section. These considerations apply in the chlorosulfonation of acetanilide (to give *N*-acetylsulfanilyl chloride, an intermediate for sulfa drugs) and of various other aromatic compounds used as dye intermediates (14). These include various chlorinated benzenes, toluenes, and dinitrobenzenes, salicylic acid, and 2-hydroxy-1-naphthoic acid. The usual industrial process comprises gradual addition of the organic compound to excess chlorosulfonic acid. The evolution of hydrogen chloride in step (1) is avoided if a mixture of chlorosulfonic acid and sulfur trioxide is used, the quantity of sulfur trioxide being equimolar with the organic reactant.

**Oxidative Procedures.** This approach is of comparatively little practical interest for the preparation of aromatic sulfonates. Aqueous chlorination of bis(*o*-nitrophenyl) disulfide has been employed industrially to prepare *o*-nitrobenzenesulfonyl chloride, an intermediate in the manufacture of orthanilic acid (1).

**Sulfite Reactions.** Direct replacement of an aromatic chlorine atom by the sulfo group is of value in special cases for preparing aromatic sulfonates. *o*-Chlorobenzaldehyde (1) and *o*-chlorobenzoic acid (14) have been converted to the sulfonates by this procedure on an industrial scale. This procedure has also been adopted for the manufacture of anthraquinonesulfonates but has not in practice extensively replaced the direct sulfonation of anthraquinone.

**Condensation Reactions.** These provide an important industrial procedure for the manufacture of polymeric aromatic sulfonates. The condensation of aqueous formaldehyde with naphthalene-2-sulfonic acid at 80–85°C. for 40 hours yields water-soluble low-molecular-weight condensation polymers useful as tanning agents (14) or as dispersing agents. Many variations of this type of reaction have been studied in the laboratory (16) and used industrially (14) to prepare tanning agents. In most cases formaldehyde is reacted with a mono- or dihydric phenol or phenolsulfonic acid or a hydrocarbon sulfonic acid in various possible ratios, in one or more steps or in several possible orders of addition depending on the types of product desired. Other variations yield water-insoluble polymers of commercial interest as ion-exchange resins (20), for example, by reacting formaldehyde, resorcinol, and benzaldehyde-2,4-disulfonic acid in aqueous solution at 100°C. All these products are of indefinite composition and are prepared by empirical procedures. (Similar products are prepared by the direct sulfonation of polystyrene or by the sulfomethylation reaction as discussed in preceding sections.)

#### HETEROCYCLIC SULFONATES

**Direct Sulfonation.** The direct sulfonation of many heterocyclic compounds (furan, pyrrole, indole, thiophene, coumarone, and many of their derivatives) has been studied extensively by Terent'ev and co-workers using pyridine- $\text{SO}_3$  (14,16,22). Yields are generally good (70–90%), the technique is simple (heating in a sealed tube at 80–140°C. in the presence or absence of a solvent such as ethylene dichloride), and the method appears widely applicable. Other sulfonating agents are unsuitable since many heterocyclic compounds decompose in the presence of acids.

Several heterocyclic sulfonates are of industrial interest. 3-Pyridinesulfonic acid, an intermediate in one process for producing nicotinic acid, can be prepared with

difficulty by heating pyridine- $\text{SO}_3$  at 225–235°C. in the presence of mercuric sulfate, or by the reaction of pyridine with 20% oleum at 250–270°C. using the same catalyst. Quinoline can be sulfonated in the benzene nucleus (5 and 8 positions) with oleum at 170–180°C.; caustic fusion of the 8-isomer yields 8-hydroxyquinoline, an important analytical reagent and fungicide. Carbazole is converted commercially to the 1,3,6-trisulfonate by heating with 95% acid at 50°C.; this sulfonate is then nitrated to yield a tetranitrocarbazole fungicide (15). The dye Quinoline Yellow Ex. is prepared (4) by heating Quinoline Yellow Spirit-Soluble (quinophthalone) with oleum at 115°C. maximum to yield a mixture of the di- and trisulfonic acids (see also *Quinoline dyes*). A dye intermediate is prepared by treating dehydrothio-*p*-toluidine (see *Thiazole dyes*) with 20% oleum to yield mainly the 7-sulfonic acid. The disulfonate was formed by further sulfonation using the baking process (1). The sulfonates of phthalocyanines (*q.v.*) are important dyes. A process study made by I. G. Farbenindustrie (5) has led to the following conclusions: (1) the monosulfonic acid is formed with 40% oleum below 20°C.; (2) with the copper, nickel, and aluminum derivatives, as well as with the metal-free compound, the disulfonic acid is formed at 51°C. with a 15-hour reaction period; (3) above 60°C. considerable trisulfonic acid is formed; (4) to introduce four sulfonic groups (as  $-\text{SO}_2\text{Cl}$ ), chlorosulfonic acid is used at 150°C. for 4–5 hours.

**Oxidative Procedures.** A series of twenty new heterocyclic sulfonyl chlorides has been prepared in the laboratory by aqueous chlorination of the corresponding thiols at 7–8°C. (26). Types of compounds studied include imidazoles, triazoles, tetrazoles, thiazoles, pyridines, and pyrazines. This approach appears broadly applicable, and of possible preparative interest for many sulfonates not otherwise easily prepared.

Other preparative procedures are of minor interest for preparing heterocyclic sulfonates. The *condensation method* has, however, been employed industrially for manufacturing phthalocyanine sulfonates using sulfophthalic acid salts as starting materials.

#### PETROLEUM SULFONATES

Sulfuric acid has been used to refine petroleum fractions for over a century, but it was not until 1875, when the manufacture of mineral white oils by drastic acid treatment of lubricant fractions with oleum was initiated, that the sulfonates so obtained as by-products became available in quantity. Two types of sulfonates were obtained: oil-soluble "mahogany acids" and oil-insoluble or water-soluble "green acids". The former type especially has found steadily increasing uses since then as emulsifiers, rust-proofing agents, and additives for heavy-duty engine lubricants to such an extent that by World War II the demand began to exceed the by-product supply, and manufacture of these sulfonates as primary products began. The water-soluble sulfonates are relatively unimportant.

Since petroleum (*q.v.*) is a complex mixture of many types of hydrocarbons of largely unknown composition and of extreme variation in ease of sulfonation from highly reactive to inert, it is not surprising that the sulfonation process, and to an even greater degree the subsequent isolation procedure, are empirical in nature and are under constant study for improvement. Three steps are involved: (1) preliminary purification of the sulfonation stock to remove sludge- and color-producing constituents either by a light treatment with sulfuric acid or, more often, by solvent extraction;

(2) the sulfonation step proper; and (3) the isolation procedure. Steps (2) and (3) will be discussed in more detail below.

In spite of its industrial importance, relatively little has been published on the sulfonation step except in patents. A survey of these indicates that a typical process may operate on a batch basis employing 20% oleum (40% by weight on the oil) applied in three successive separate treatments ("dumps") with a reaction time of 1-3 hours in the temperature range 40-70°C. The yield of mahogany sulfonate may be 5-10 grams per 100 grams of original base stock. The sulfonation can also be operated continuously. Sulfur trioxide vapor can be advantageously substituted for oleum as the sulfonating agent.

The third step may comprise: (1) separation from the associated spent acid, sludge, and unreacted oil; (2) purification (including decolorization and deodorization); and (3) conversion to various metallic salts of commercial utility. The many patented processes on these steps have been reviewed (6,11,14-16,21-23); it is doubtful whether many of these are in actual commercial operation. For some uses, the mahogany sulfonates are simply converted to the desired metallic salt without separation from the residual unsulfonated oil. Alcohol extraction yields a more concentrated sulfonate still containing much oil (about 50%). Further purification, yielding an essentially oil-free metallic sulfonate, can be realized by treating the alcoholic extract with petroleum ether to effect de-oiling, followed by distillation of the alcohol. Purification of the green sulfonates is more complicated.

The chemical composition of petroleum sulfonates has been studied by Sperling (29), who found major differences between the two classes of sulfonates using the technique of hydrolytic desulfonation discussed in a preceding section. A summary of his findings is presented in Table II.

TABLE II. Comparison of Mahogany and Green Sulfonates.

	"Mahogany"	"Green"
Hydrocarbon type	Long aliphatic chain, small ring system	Short aliphatic chains, polycyclic ring systems
Disulfonate content	Nil	About one-third
Composition of hydrolyzate		
Hydrocarbons	97.24%	44.5-67.8%
Mean molecular weight	341	232-297
Stability (to heat and oxidation)	Stable	Unstable
Oxidation products	2.76%	55.5 to 28.6%
Method of formation	Direct aromatic sulfonation	Dehydrogenation (oxidation) of cycloparaffin, followed by sulfonation of the cyclohexane type; also some direct aromatic sulfonation

It will be noted that the mahogany sulfonates are structurally similar to the dodecylbenzenesulfonates; and that the sulfonating agents (20% oleum and sulfur trioxide vapor) and the process conditions are also comparable. Side reactions predominate in the formation of the green sulfonates, oxidation and polysulfonation being outstanding. Molecular rearrangement, possibly in part of the Jacobson type, is no doubt extensive. The susceptibility to oxidation of the hydrocarbons obtained by

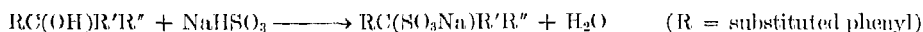
hydrolytic desulfonation of the green acids is so great that they were given serious commercial consideration at one time as possible synthetic drying oils (10).

The residual unsulfonated oil (mineral white oil) from the above process is very resistant to further sulfonation with oleum or sulfur trioxide, but further sulfonation can be readily achieved by sulfochlorination.

#### LIGNIN SULFONATES

The production of pulp (*q.v.*) by heating wood under pressure with an aqueous solution of metallic bisulfite and sulfur dioxide (sulfite cooking acid) yields water-soluble lignin sulfonates as a major by-product. These materials, available to the extent of millions of tons annually, have found uses to a minor extent as dispersing agents, raw materials for manufacturing vanillin, tanning agents, ion-exchange resins and other purposes (see *Lignin*).

The structure of lignin is not known, but it appears to comprise a mixture of polymers containing aromatic rings, methoxyl groups, hydroxyl groups (both phenolic and alcoholic), and carbonyl groups. For a possible structural formula of a lignin monomer unit, see Vol. 8, p. 329. Correspondingly, the chemical structure of the sulfonate is not known, although it has been under continued and intensive investigation for a considerable period of time and with application of a variety of approaches and techniques (14-16). The reaction may proceed stepwise with the formation of at least three types of sulfonates depending upon the conditions used, especially the pH of the reaction mixture. Treatment of pure chemical compounds of types thought to be present in the lignin molecule ("lignin models") with sulfite cooking acid under simulated commercial conditions has shown that a hydroxyl group alpha to the benzene nucleus is replaced by a sulfonate group as follows:



This reaction occurs with veratryl alcohol (3,4-dimethoxybenzyl alcohol) and related lignin models, leading to the conclusion that lignin sulfonates may be formed in part by similar reactions.

#### "SULFONATED" FATTY OILS

The manufacture of the so-called sulfonated oils from fatty glycerides or acids containing olefinic or hydroxyl groups or both (for example, castor, soybean, peanut, and various fish oils) has steadily increased since 1875, when sulfonated castor oil (Turkey-red oil; see Vol. 3, p. 240) was introduced as the first commercial sulfonate-type textile assistant. These products have long been prepared industrially by largely empirical methods involving direct treatment of the oil (or derived ester, acid, etc.) with sulfur trioxide or a related compound (sulfuric acid, oleum, chlorosulfonic acid, acetyl sulfate, etc.), thereby introducing hydrophilic sulfate or sulfonate groups or both. They comprise complicated mixtures of sulfated oil, sulfated or sulfonated acids, sulfuric acid esters, hydroxy acids, estolides, lactides, polymeric substances, and other compounds depending upon the raw materials and conditions used (see Vol. 6, p. 220) (24,25,27).

The usual process conditions comprise gradual addition of cold concentrated acid to the oil with good agitation and cooling in a batch operation using a lead, Monel, or nickel-clad steel reaction kettle (14,19). Subsequent operations involve separation of spent acid and neutralization of the sulfonate. A summary of reaction conditions

used in commercial and laboratory practice is presented in Table III. Numerous variations have appeared in the patent literature (25,27), but it seems doubtful that many of these are applied in practice.

The chemical reactions occurring during fatty oil "sulfonation" will depend upon various factors. The most common reaction is probably sulfation of a double bond (addition of H and  $-\text{OSO}_2\text{OH}$ ) or a hydroxyl group by the concentrated acid. Oleum and sulfur trioxide react in the various possible ways discussed in a preceding section to yield ultimately hydroxy sulfonates, whereas chlorosulfonic acid will form either a sulfate or a sulfonate depending upon conditions. In addition, many side reactions occur which do not involve the introduction of sulfur into the organic molecule; these products in turn can also undergo "sulfonation" in various possible ways. Evidently, the chemistry of fatty oil "sulfonation" is as complex as the actual manufacturing process is simple.

The formation of the important monoglyceride sulfate detergents by the direct reaction of glycerol, oleum and a triglyceride, a process comparable in its simplicity to that of fatty oil "sulfonation," is discussed below under "Sulfation." The sulfonation of saturated fatty acids with sulfur trioxide is considered under "Aliphatic Sulfonates."

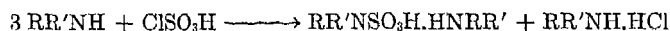
TABLE III. Reaction Conditions for the Preparation of "Sulfonated" Fatty Oils.

Oil	Lb. sulfonating agent <sup>a</sup> per lb. oil	Time, hr.	Temp., °C.	Reference
Castor	0.25	3	30	14
Castor	0.21	9	25-30	14
Butyl ricinoleate	1.0	6.5	0	14
Shark	0.2	3	25	14
Sperm	0.09	3	25	14
Neat's foot	0.10	> 2	15-24	14
Cod	0.12	—	7-18	14
Oleic acid	0.57	3	5-10	13
<i>N</i> -Ethylanilide of oleic acid	Approx. 1	10-15	0	14

<sup>a</sup> Concentrated sulfuric acid used in all cases except those of oleic acid (solution of sulfur trioxide in tetrachloroethylene) and its *N*-ethylanilide (100% acid).

#### *N*-SULFONATES (SULFAMATES)

The most important procedures for sulfonation on nitrogen (7) may be classified under the same four headings as those for sulfonation on carbon. Likewise, as for sulfonation on carbon, the most widely applicable of the four methods involves treatment of an amine (primary, secondary, or tertiary) or an amide with sulfur trioxide or a compound thereof (for example, chlorosulfonic acid, sulfur trioxide complexes, sulfuryl chloride, acetyl sulfate, or sulfamic acid, but not sulfuric acid or oleum). A favored reagent is chlorosulfonic acid (7,8), which reacts according to the equation:



This approach has been used commercially for producing sodium di(*n*-butyl)-sulfamate, a textile mercerizing assistant, and sodium cyclohexylsulfamate, a sweetening agent. An interesting laboratory procedure for separating *o*- from *p*-ethylaniline involves preferential *N*-sulfonation of the para isomer with triethylamine- $\text{SO}_3$ . The naturally occurring blood anticoagulant heparin (see p. 336) contains sulfamic acid linkages.

Sulfamic acid (*q.v.*) is manufactured by treating urea with pyrosulfuric acid:



This acid finds application as a sulfating agent for alcohols and, in the form of its ammonium salt, as an herbicide.

The direct reaction of ammonia with sulfur trioxide has been studied extensively by commercial research laboratories. A mixture of compounds is formed, including ammonium sulfamate and sulfamide ( $\text{NH}_2\text{SO}_2\text{NH}_2$ ) (16).

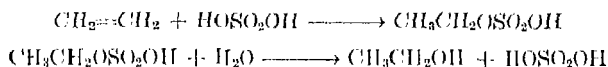
### Sulfation

Sulfation involves the placement of an  $-\text{OSO}_2\text{OH}$  grouping on carbon; in some cases it can be regarded as the placement of an  $-\text{SO}_2\text{OH}$  group on oxygen. Types of compounds sulfated are almost entirely limited to those containing olefinic unsaturation (principally alkenes), and those with hydroxyl groups, either phenolic or alcoholic, together with the ethers of the latter. Furthermore, sulfation procedures are confined to the one general method of treating these types of compounds with sulfur trioxide or an appropriate compound thereof. For alkenes, concentrated sulfuric acid is usually employed, whereas, for alcohols, chlorosulfonic acid, oleum, or sulfur trioxide complexes are commonly used. It is noteworthy that sulfations can be conducted in aqueous solutions when using amine- $\text{SO}_3$  complexes.

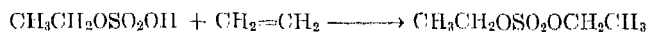
Sulfates have important uses as intermediates for preparing alcohols (ethyl, isopropyl, etc.), and as alkylating agents (dimethyl and diethyl sulfates; see *Sulfuric and sulfurous esters*), detergents (sodium lauryl sulfate), dyes, and blood anticoagulants. Sulfation is a predominant reaction in the "sulfonation" of fatty oils, as indicated in a preceding section.

Equipment employed in industrial sulfations is of standard types and may be similar to that used for sulfonation as discussed in a preceding section. Evolution of hydrogen chloride from alcohols when sulfated with chlorosulfonic acid presents problems of corrosion and also of waste disposal, unless the hydrogen chloride is reacted with sulfur trioxide to regenerate chlorosulfonic acid. The sulfation of the lower alkenes (for alcohols), of the higher alkenes (for detergents), and of lauryl alcohol has reached sufficient manufacturing volume to make the adoption of continuous processes attractive. The production of dimethyl sulfate (from dimethyl ether and sulfur trioxide) is also well suited to continuous operation.

**Sulfated Alkenes.** The sulfation of the lower alkenes derived from petroleum, in particular, ethylene, propylene, butylenes, and pentylenes, is an operation of established commercial importance for production of the corresponding alcohols. As typified by the preparation of ethyl alcohol, the reactions are:



Diethyl sulfate is formed by a side reaction:



Sulfation of long-chain alkenes ( $\text{C}_{12}$ – $\text{C}_{18}$ ) is operated commercially in Europe for the production of detergents and wetting agents (9) using hydrocarbons obtained either by the cracking of paraffin wax or from shale oil. The sulfation is carried out at 10–15°C., in 90–96% acid, an acid-to-alkene molar ratio of approximately 2:1 being used. Short

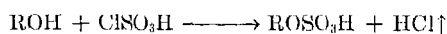
contact time and efficient mixing are essential. Working-up involves tar removal (by centrifuging), breakdown of undesired dialkyl sulfates (by holding at 90°C. for 8 hours with aqueous sodium carbonate), and removal of unreacted hydrocarbons (by solvent extraction). This type of detergent is not manufactured in the U.S., where the dodecylbenzene type is preferred.

**Alcohol Sulfates.** Dimethyl sulfate can be manufactured in excellent yield and purity by the continuous reaction of dimethyl ether and sulfur trioxide:



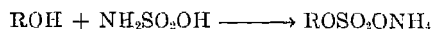
The process involves simple countercurrent mixing of the reactants in an aluminum tower, charged with reaction product, at 40°C. with moderate external cooling. Dimethyl ether is available as a by-product of methanol synthesis.

The sulfation of long-chain alcohols is of great technical importance for the production of detergents and wetting agents, especially sodium lauryl sulfate, notable as the first practical synthetic detergent. A comprehensive general summary of the various alcohols used, of suitable sulfating agents, and of the patent situation is available (27). A review of commercial operating procedures (14) shows chlorosulfonic acid to be the preferred sulfating agent for the saturated fatty alcohols (lauryl, cetyl); it is also used for unsaturated ones (oleyl, sperm oil alcohols). The technique involves addition of the sulfating agent to the alcohol with or without a solvent such as chloroform or carbon tetrachloride, while maintaining the reaction temperature at 25–30°C. Hydrogen chloride is evolved according to the equation:



The saturated fatty alcohols can be sulfated with dilute sulfur trioxide vapor without use of a solvent (17). Oleyl alcohol, because of the complicating factor of possible sulfation of the double bond, is sulfated industrially by several procedures, the one used depending upon empirical use performance tests with the product. Reagents used (14) include chlorosulfonic acid,  $\text{ClSO}_3\text{H}$ , mixed with formamide and urea, monohydrate acid (100%  $\text{H}_2\text{SO}_4$ ) (below 30°C.), 97% acid (at 40–45°C.), and pyridine- $\text{SO}_3$ ; the last reagent gives minimum attack of the double bond.

The sulfation of alkylphenol polyglycol ethers (reaction products of alkylated phenols with ethylene oxide) is best conducted by heating at 120–125°C. with sulfamic acid as follows:



Such products have been marketed commercially as detergents (Alipals).

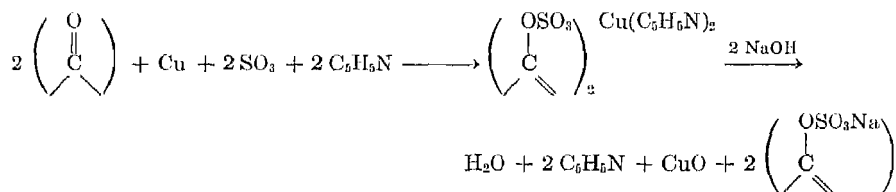
The mechanism and rate of the sulfation of primary and secondary alcohols with sulfuric acid has been studied (15). The former react ten times faster than the latter, with the reaction postulated as proceeding without alkyl-oxygen cleavage in a manner similar to carboxylic acid esterification.

The fatty monoglyceride sulfates ( $\text{RCOO}(\text{CH}_2\text{CHOHCH}_2\text{OSO}_2\text{ONa})$ ;  $\text{RCO}$  may be any fatty acid radical as in the common triglycerides) have been manufactured for many years as industrial detergents (27) by a one-step process involving mixing the glyceride (1 mole), glycerol (2 moles), and sulfuric acid or oleum (in excess). Alcoholysis occurs as well as sulfation. Although these sulfates are simple to manufacture and are perhaps the cheapest of the fat-based synthetic detergents, they are chemically unstable and are not easily produced in the desired high active form. Consequently, they have been partially replaced by the dodecylbenzenesulfonate detergents.

**Sulfates of Ring Compounds.** Amine-SO<sub>3</sub> complexes are the principal sulfating agents for this category, which includes phenolic compounds, steroid derivatives, and the leuco (or dihydroxy) form of vat dyes. The first two types of sulfates have a biological interest, since phenols and sterols are excreted from the body in this chemical form; the third type is manufactured in quantity.

Preferential sulfation of individual phenols in mixtures (for example, *o*- and *p*-phenylphenols, 5- and 8-benzamido-1-naphthols) with triethylamine-SO<sub>3</sub> forms a basis for their separation. The aromatic sulfates are stable in neutral or alkaline solution and are not affected by the oxidation or reduction of other groupings in the molecule. Also, the sulfates are water-soluble and the sulfate group is easy to introduce and remove. Consequently, sulfation has sometimes been used to block phenolic hydroxyl groups before the oxidation of various organic compounds.

Combined reduction and sulfation of vat dyes, especially the anthraquinone dyes, has been increasingly used in industry since 1924 to achieve water solubility with consequent easy application to textile fibers (see Vol. 1, p. 976). The reaction is conducted by heating the dye with a metal (copper, iron, or zinc) and pyridine-SO<sub>3</sub> (or other amine complexes) by the following schematic reactions:



Oxidation of the organic sodium sulfate in acid solution reconverts it to the original insoluble form of the dye, thereby fixing it on the textile fiber. This direct and widely applicable procedure is used to produce over 50 individual dyes. Details of current manufacturing practice and a review of the broad scope of the reaction have been published (34). A more recent variation of this procedure involves preliminary reduction of the vat dye in aqueous solution to the leuco (hydroxy) form, followed by sulfation in the same solution with amine-SO<sub>3</sub>.

**Sulfated Carbohydrates and Nitrogenous Polysaccharides.** Sodium cellulose sulfate, prepared by the treatment of cellulose with sulfuric acid and containing approximately one sulfate group per three anhydroglucose units, was produced for some time on a semicommercial scale. The reaction was so conducted that no degradation occurred during sulfation. This is possible in the presence of an aliphatic alcohol at a temperature below 15°C. Water solutions of the product are viscous, suggesting possible applications as a synthetic water-soluble gum like those of sodium carboxymethylcellulose. Similar products may be prepared by the sulfoalkylation of alkali cellulose with sodium 2-chloroethanesulfonate. Starch yields comparable derivatives.

The sulfates of naturally occurring amine derivatives of polysaccharides (*q.v.*), have attracted considerable biochemical interest because *heparin*, the potent blood anticoagulant, falls in this category. Recent work has shown that heparin contains both sulfamate and sulfate groups, the former type probably contributing more to its biological activity. A variety of polyhydroxy compounds, many also containing amino groups, have been sulfated experimentally to varying degrees, usually with pyridine-SO<sub>3</sub>, in an effort to prepare materials with activity similar to that of heparin.



These have included chitosan, *N*-deacetylated chitin and chondroitinsulfuric acid, polyuronic acids, alginic acid, dextrin, pectin, and mucicetin. Both sulfamation and sulfation occur in compounds containing amino groups. In most cases the anticoagulant activity obtained was inferior to that of heparin. Degradation sometimes occurred during sulfation.

### Bibliography

- (1) Adams, D. A. W., *et al.*, *U.S. Dept. Commerce, OTS Rept.*, PB 85,687 (1946).
- (2) Alexander, E. R., *Principles of Ionic Organic Reactions*, Wiley, N.Y., 1950, p. 252.
- (3) Andrews, D. B., *et al.*, *FIAT Final Rept. No. 1313* (PB 85,172), U.S. Dept. Commerce, 1948, Vol. I, p. 100.
- (4) *Ibid.*, Vol. II, p. 384.
- (5) *Ibid.*, Vol. III, pp. 304-8.
- (6) Archibald, F. M., "Sulpho Acids," in Dunstan, Nash, Brooks, and Tizard, eds., *The Science of Petroleum*, Vol. IV, Oxford University Press, N.Y., 1938, pp. 2837-40.
- (7) Audrieth, L. F., and Sveda, M., *J. Org. Chem.*, **9**, 89 (1944).
- (8) Audrieth, L. F., Sveda, M., Sisler, H. H., and Butler, M. J., *Chem. Revs.*, **26**, 49 (1940).
- (9) Birch, S. F., *J. Inst. Petroleum*, **38**, 69 (1952).
- (10) Bornstein, L., and Rostler, F., *Modern Plastics*, **19** [8], 72-4, 122 (1942).
- (11) Ellis, C., *The Chemistry of Petroleum Derivatives*, Vol. II, Reinhold, N.Y., 1937, pp. 1064-86.
- (12) Englund, S. W., Aries, R. W., and Othmer, D. F., *Ind. Eng. Chem.*, **45**, 189 (1953).
- (13) General Chemical Division, Allied Chemical & Dye Corp., *Tech. Service Bull.*, SF-3, 1951.
- (14) Gilbert, E. E., and Jones, E. P., *Ind. Eng. Chem.*, **43**, 2022 (1951).
- (15) Gilbert, E. E., and Jones, E. P., *Ind. Eng. Chem.*, **44**, 2082 (1952).
- (16) Gilbert, E. E., and Jones, E. P., *Ind. Eng. Chem.*, **45**, 2041 (1953).
- (17) Gilbert, E. E., Veldhuis, B., Carlson, E. J., and Giolito, S. L., *Ind. Eng. Chem.*, **45**, 2065 (1953).
- (18) Groggins, P. H., "Sulfonation," in Groggins, ed., *Unit Processes in Organic Synthesis*, 4th ed., McGraw-Hill, N.Y., 1952, p. 266.
- (19) Hilditch, T. P., *The Industrial Chemistry of the Fats and Waxes*, 2nd ed., Van Nostrand, N.Y., 1941, p. 400.
- (20) Kunin, R., and Myers, R. J., *Ion Exchange Resins*, Wiley, N.Y., 1950.
- (21) Lisk, G. F., *Ind. Eng. Chem.*, **40**, 1671 (1948).
- (22) Lisk, G. F., *Ind. Eng. Chem.*, **41**, 1923 (1949).
- (23) Lisk, G. F., *Ind. Eng. Chem.*, **42**, 1746 (1950).
- (24) Markley, K. S., *Fatty Acids*, Interscience, N.Y.-London, 1947, pp. 521 ff.
- (25) Ralston, A. W., *Fatty Acids and Their Derivatives*, Wiley, N.Y., 1948, pp. 459 ff.
- (26) Roblin, R. O., Jr., and Clapp, J. W., *J. Am. Chem. Soc.*, **72**, 4890 (1950).
- (27) Schwartz, A. M., and Perry, J. W., *Surface Active Agents*, Interscience, N.Y.-London, 1949.
- (28) Snell, F. D., Allen, L. H., and Sandler, R. A., *World Petroleum Congr. Proc.*, 3rd Congr., Hague, 1951, Sect. V, pp. 109-18.
- (29) Sperling, R., *Ind. Eng. Chem.*, **40**, 890 (1948).
- (30) Sperling, R., *J. Chem. Soc.*, **1949**, 1925-7, 1932-9.
- (31) Suter, C. M., *The Organic Chemistry of Sulfur*, Wiley, N.Y., 1944.
- (32) Suter, C. M., Evans, P. B., and Kiefer, J. M., *J. Am. Chem. Soc.*, **60**, 538 (1938).
- (33) Suter, C. M., and Weston, A. W., "Direct Sulfonation of Aromatic Hydrocarbons and Their Halogen Derivatives," in Adams, Bachmann, Fieser, Johnson and Snyder, eds., *Organic Reactions*, Vol. III, Wiley, N.Y., 1946, pp. 141 ff.
- (34) Venkataraman, K., *The Chemistry of Synthetic Dyes*, Vol. II, Academic Press, N.Y., 1952, pp. 1046 ff.
- (35) Wheaton, R. M., and Harrington, D. F., *Ind. Eng. Chem.*, **44**, 1796 (1952).

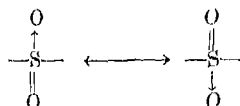
E. E. GILBERT

**SULFONEPHTHALEINS.** See *Sulfur compounds, organic*.

## SULFONES

In general sulfones are characterized by the union of the sulfonyl group,  $-\text{SO}_2-$ , and two carbon atoms (general formula  $\text{R}_2\text{SO}_2$ ), although a special class, the  $\alpha$ -disulfones, possess the structure  $\text{C}-\text{SO}_2-\text{SO}_2-\text{C}$ .  $\beta$ -Disulfones,  $\text{C}-\text{SO}_2-\text{C}-\text{SO}_2-\text{C}$ ,  $\gamma$ -disulfones, etc., and cyclic sulfones are also known.

The nature of the sulfur-oxygen bond in sulfones and sulfoxides has been the subject of many investigations. The conflicting results indicate that both double and semipolar (dative) bonds contribute to resonance (2,39) as, for example:



Thus evidence has been found for double bonds or against semipolar bonds in studies based on electric moments (29), molecular orbits (27), electron diffraction (24), infrared (2,3) and x-ray analyses (39), and on conjugation occurring when a sulfonyl group is adjacent to double bonds, a lone pair of electrons, or C—H bonds (4,11,19,20). On the other hand, data indicating a semipolar structure have been obtained from parachor and molecular refraction studies (31,36a,40,41), copolymerization studies (30,32,33), ultraviolet absorption (30,32,33), and infrared absorption (31). See also *Sulfur compounds—structure*.

The x-ray data indicate that sulfur in bis (*p*-bromophenyl) sulfone is approximately tetrahedral with a C—S—C valence angle of approximately  $100^\circ$ , a value comparable to the angle  $102 \pm 4^\circ$  obtained from dipole measurements of phenyl sulfone (22). The data also indicate that the benzene rings are perpendicular to the Br—S—Br plane.

In general, spectral analysis gives no indication of a characteristic absorption band for the isolated sulfone group in the ultraviolet, but two characteristic infrared bands have been noted at  $1,120$ – $1,160 \text{ cm.}^{-1}$  and  $1,300$ – $1,350 \text{ cm.}^{-1}$  (35).

Sulfones are commonly named like ethers or sulfides by means of hydrocarbon radicals; for example,  $\text{CH}_3\text{SO}_2\text{CH}_3$ , methyl sulfone or dimethyl sulfone. According to the I.U.P.A.C. system, they are named as substitution products, as  $\text{CH}_3\text{C}(\text{SO}_2\text{CH}_3)_2\text{CH}_2\text{CH}_2\text{C}(\text{SO}_2\text{CH}_3)_2\text{CH}_3$ , 2,2,5,5-tetrakis(methylsulfonyl)hexane. The prefix sulfonyl is also used for sulfones containing certain other functional groups, such as  $\text{SO}_2(\text{CH}_2\text{COOH})_2$ , sulfonyldiacetic acid. Sulfones derived from cyclic or other complicated sulfides are often designated "dioxides," for example, thiophene 1,1-dioxide (or *S*-dioxide).

## Physical Properties

The sulfones are normally stable, crystalline substances of high boiling point, but certain members exist as liquids and others decompose on heating (see Table I). The lower members, such as ethyl sulfone, are moderately soluble in water, but even such simple compounds as *n*-butyl sulfone are insoluble.

## Reactions

The reactions of the sulfones may be divided into three broad classes: reactions at the sulfonyl group; reactions induced in adjoining groups by the sulfonyl group; and reactions that are characteristic of specific types of sulfones.

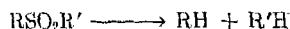
TABLE I. Physical Constants of Various Sulfones.

Sulfone	M.p., °C.	B.p., °C.
(CH <sub>3</sub> ) <sub>2</sub> SO <sub>2</sub>	109	238
(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> SO <sub>2</sub>	74	248
( <i>n</i> -C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> SO <sub>2</sub>	25	142 <sub>25</sub>
ClCH <sub>2</sub> SO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	33	128 <sub>14</sub>
(ClCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> SO <sub>2</sub> (mustard sulfone)	56	—
(C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> ) <sub>2</sub> SO <sub>2</sub>	151	—
C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	42	—
<i>p</i> -BrC <sub>6</sub> H <sub>4</sub> SO <sub>2</sub> CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	159	—
2,4-(NO <sub>2</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> SO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	160	—
(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> SO <sub>2</sub>	128	379
(2-C <sub>10</sub> H <sub>7</sub> ) <sub>2</sub> SO <sub>2</sub>	177	—
(1-C <sub>10</sub> H <sub>7</sub> ) <sub>2</sub> SO <sub>2</sub>	187	—
<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> SO <sub>2</sub> CH <sub>2</sub> OH	90	—
<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> SO <sub>2</sub> CHOHCH(CH <sub>3</sub> ) <sub>2</sub>	Dec. in air	—
2-C <sub>10</sub> H <sub>7</sub> SO <sub>2</sub> C(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CN	Transparent resin	—
C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub> CH <sub>2</sub> COCl <sub>2</sub> Br	96	—
C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub> CH <sub>2</sub> CH=CH <sub>2</sub>	Oil	—
<i>p</i> -CH <sub>3</sub> SO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> NHNH <sub>2</sub>	136	—
C <sub>2</sub> H <sub>5</sub> SO <sub>2</sub> CH <sub>2</sub> CONH <sub>2</sub>	99	—
(C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub> ) <sub>2</sub>	193-94	—
CH <sub>3</sub> SO <sub>2</sub> CH <sub>2</sub> SO <sub>2</sub> CH <sub>3</sub>	143	—
C <sub>2</sub> H <sub>5</sub> SO <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> SO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	137	—
(CH <sub>3</sub> ) <sub>2</sub> C(SO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (sulfonal)	126	—
CH <sub>3</sub> C(C <sub>2</sub> H <sub>5</sub> )(SO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (trional)	76	—
( <i>p</i> -NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> ) <sub>2</sub> SO <sub>2</sub> (DDS)	108	—

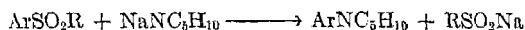
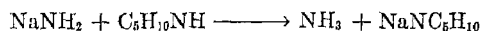
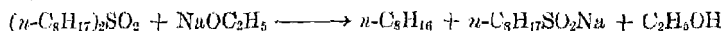
**Reactions at the Sulfonyl Group.** In most instances, reduction of sulfones to the corresponding sulfides (*q.v.*) is accomplished with difficulty and only lithium aluminum hydride appears to have general applicability (6). This agent accomplishes the reduction of five-membered ring compounds at 35°C., but higher temperatures are required for the reduction of six-membered ring compounds, open-chain compounds, and phenyl sulfones.

Other agents employed with variable, though by no means general, success, are zinc (15), tin (42), hydrogen sulfide (18), and sulfur.

In some instances chemical reductions result in cleavage, and pyrophoric nickel has been represented as applicable for this purpose (55). This agent effects conversion to the hydrocarbons:



Cleavage is also frequently accomplished by alcoholic sodium ethoxide (12) or by sodamide in piperidine (7):



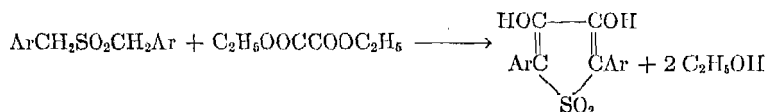
In some instances cleavage may be produced by fused 90% potassium hydroxide, but higher aliphatic sulfones such as *n*-octyl are unaffected by this agent. Dilute alkali is usually ineffective but it smoothly removes one sulfonyl group from a  $\gamma$ -disulfone, and when applied to the nitroaryl aminoaryl sulfones (44) or the *o*-hydroxyaryl sulfones (14) yields sulfonic acids by fission and rearrangement (see below).

A number of electrophilic agents such as halogens (in the absence of substitution catalysts) and phosphorus pentachloride have been observed to cleave certain sulfones, but again the effect is dependent upon the nature of the sulfone. Methyl ethyl sulfone, for example, is unreactive toward phosphorus pentachloride, but phenyl sulfone yields chlorobenzene and benzenesulfonyl chloride with this agent.

If the sulfone bears unsaturated groups (see p. 342), addition reactions rather than cleavage may occur, and aromatic sulfones yield nuclear substitution products if reacted with halogens in the presence of substitution catalysts such as iodine.

**Reactions Induced by the Sulfonyl Group.** The sulfonyl group is meta-directing in substitution reactions of aromatic nuclei, nitration of phenyl sulfone, for example, yielding bis(*m*-nitrophenyl) sulfone. Like other meta-directing groups, the sulfonyl group activates halogens in ortho and para positions and permits them to react in metalthesis, although it is less effective in this respect than the nitro group (38). Bordwell and Cooper have investigated the effect of the methylsulfonyl group in the meta and para positions and have concluded that an appreciable resonance effect is involved (4).

Like the nitro group, the sulfonyl group activates adjacent methylenic hydrogen atoms, but again the effect is not comparable to that produced by a nitro group. Several arylmethyl sulfones have been observed to condense with ethyl oxalate to yield the 2,5-diaryl-3,4-dihydroxythiophene dioxides (28), for example, but such compounds as benzyl sulfone or phenyl benzyl sulfone fail to enter into alkylation reactions with methyl iodide (36):



However, the presence of an additional activating group such as carbonyl, carbalkoxy (alkoxycarbonyl), cyano, amido, or sulfonyl markedly augments the effect of a single sulfonyl group. Bis(ethylsulfonyl)ethane, for example, is readily alkylated and halogenated at the methylenic carbon.

Carboxylic acids bearing a sulfonyl group in the alpha position are stronger acids than the corresponding aliphatic acids from which they are derived (26). The influence of the sulfonyl group in this position is also reflected in the ease with which such acids are decarboxylated, but a sulfonyl group in the beta position has no apparent effect upon the stability of the acid.

#### CHARACTERISTIC REACTIONS OF SPECIFIC TYPES OF SULFONES

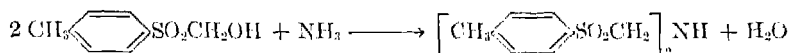
**Halogenated Sulfones.** When situated alpha to a sulfonyl group, a halogen is relatively unreactive in metathesis, but it is readily removed by reduction. The ease of reduction is illustrated by the failure of  $\alpha$ -halogenated sulfones to yield  $\beta$ -disulfones by metathesis with a sulfinate—reduction rather than metathesis occurs:



In the beta position, halogen undergoes many of the usual double decomposition reactions of alkyl halides (8,9). However, neither these nor any other halogenated sulfones have been observed to form a Grignard reagent, but Grignard reagents of the sulfones have been prepared indirectly (13,21,45). Little information is available regarding the behavior of  $\gamma$ - or  $\delta$ -halogenated sulfones.

As previously noted, halogens are activated when they are ortho or para to a sulfonyl group in an aromatic nucleus and may enter into certain double-decomposition reactions.

**Hydroxy Sulfones.** A few  $\alpha$ -hydroxy sulfones, all relatively unstable, are known. Some compounds of this class react with ammonia or with aniline to yield the substituted  $\alpha$ -amino sulfone:



However, sulfones of the type  $\text{ArSO}_2\text{CHOHAr}$  are decomposed in these reactions.

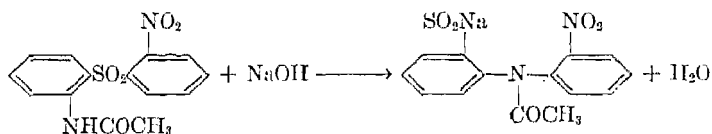
$\beta$ -Hydroxy sulfones are generally quite stable and resistant to peroxide oxidation. They react normally with phosphorus pentachloride and hydrochloric acid to yield the chloride and with sulfuric acid to yield the ether or the acid sulfate according to conditions.

The aromatic *o*-hydroxy sulfones are of interest in that certain members undergo rearrangement in dilute alkali to yield salts of the isomeric ethers of sulfinic acids (14,17,43):

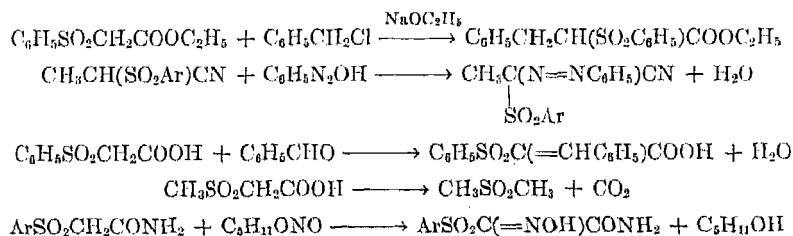


However, the *p*-hydroxy sulfones undergo fission under such treatment.

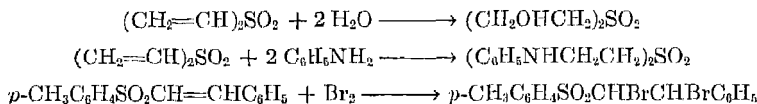
**Amino Sulfones.**  $\alpha$ -Amino sulfones are rare and unstable inasmuch as they are formed from  $\alpha$ -hydroxy sulfones (see above).  $\beta$ -Amino sulfones, on the other hand, are stable and well known and in fact may be prepared by oxidation of the amino sulfides (34). The aminoaryl sulfones undergo the usual reactions of aromatic amines, for example, they may be acylated or diazotized. However, aryl sulfones containing an *o*-amino group in one ring and an *o*-nitro group in the second ring undergo rearrangement in dilute alkali to yield sulfinates of diarylamines (49), a reaction comparable to that described above for the *o*-hydroxyaryl sulfones:



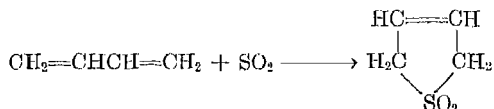
**Sulfonyl Derivatives of Acids and Related Compounds.** This class includes such substances as the sulfonyl-substituted acids, esters, amides, and nitriles. The ease of decarboxylation of  $\alpha$ -sulfonyl carboxylic acids and the activating effect of the sulfonyl group upon adjacent methylenic hydrogen atoms when augmented by carbalkoxy, cyano, amido, and carboxyl groups has already been noted. The following reactions are illustrative of this behavior:



**Unsaturated Sulfones.** An olefinic group immediately adjacent to a sulfonyl group is resistant to hydrogen peroxide and related oxidations. This behavior has permitted the synthesis of a number of vinyl sulfones by oxidation of the corresponding unsaturated sulfides (23). Such unsaturated sulfones are remarkably reactive with such reagents as bromine, hydrogen bromide, mercaptans, amines, and alcohols. However, the individual sulfones differ in reactivity:



Allyl sulfones have likewise been prepared by peroxide oxidation of the unsaturated sulfides, but such compounds are more commonly prepared by metathesis, using the sulfinate and an allyl halide. The reactions of the allyl sulfones with bromine, chlorine, and the hydrogen halides are normal. The unsaturated cyclic sulfones are best represented by the thiacyclo-3-pentene 1,1-dioxides (the 2,5-dihydrothiophene *S*-dioxides) which are obtained from conjugated dienes and sulfur dioxide:



These compounds react at the olefinic bond by addition with alcohols, amines, phenols, and halogens. Hydrolysis of the halogen addition product yields a glycol which is isomeric with that obtained by direct oxidation of the olefinic bond with permanganate. Presumably the diol obtained from the dihalide bears a *trans* configuration and that from direct oxidation a *cis* configuration in keeping with the normal behavior of olefinic systems.

Sulfones of this class are moderately stable compounds but may be decomposed on heating, with regeneration of the diolefins. This characteristic has permitted industrial application in the isolation of conjugated dienes (see "Uses"). In certain instances, these sulfones are isomerized to the thiacyclo-2-pentene 1,1-dioxides under the influence of ultraviolet light and basic catalysts.

Other thiophene derivatives have been prepared and investigated. The sulfone of thienessal(tetraphenylthiophene) has been prepared by hydrogen peroxide oxidation. The derivative benzothiophene 1,1-dioxide has been observed to undergo a variety of addition reactions in the 2,3-position (5).

**Disulfones.** Two noteworthy characteristics of the disulfones, the hydrolysis of  $\gamma$ -disulfones and the reactivity of methylenic hydrogen atoms of  $\beta$ -disulfones, have already been noted.  $\gamma$ -Disulfones are differentiated from other disulfones by the ease with which they are hydrolyzed to the hydroxy monosulfones (*Stuffer's rule*).

### Preparation

Five classes of preparative methods are described below. The first four are of general application, but the last class includes methods employed for specific types of sulfones.

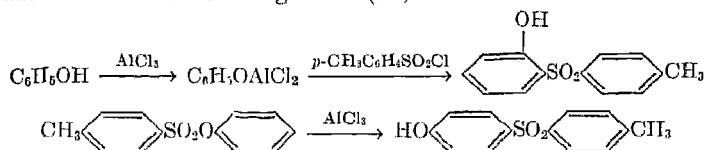
**Oxidation.** Organic sulfides (*q.v.*) react with a variety of oxidants such as nitric acid, chromic acid, hypochlorites, organic peroxides, and hydrogen peroxide to yield either sulfoxides or sulfones according to conditions. In general, the oxidation is

conveniently achieved by use of 30% hydrogen peroxide in glacial acetic acid; however, peroxy acids react at a much faster rate and give products in many cases where hydrogen peroxide fails; ruthenium tetroxide has recently been recommended as an effective oxidant (10).

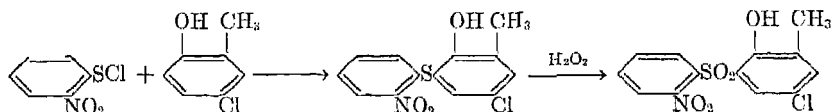
Oxidative methods are applicable not only to the synthesis of saturated, unsubstituted sulfones but may also be used for the preparation of substituted sulfones including those possessing such groups as substituted phenolic, 2-hydroxyalkyl, 2-aminoalkyl, allyl, and vinyl.

**Metathesis from Sulfinates.** Alkali metal or silver sulfinates have been treated with a variety of halogenated compounds to yield sulfones. On occasion, potassium or allyl sulfates or certain active aromatic nitro compounds have been employed with approximately the same effect as a halide. Among the compounds prepared by this method are the unsubstituted saturated sulfones, the allyl sulfones, the alkylsulfonyl and arylsulfonyl carboxylic acids (as well as related compounds such as the esters, amides, and nitriles), and  $\alpha$ - and  $\gamma$ -disulfones.

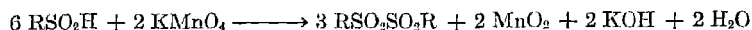
**The Friedel-Crafts and Related Reactions.** A variety of alkyl aryl sulfones and diaryl sulfones may be prepared by the action of a sulfonyl halide on an aromatic nucleus in the presence of aluminum or ferric chloride, but the method is of greatest effectiveness in the preparation of the diaryl sulfones. The method may also be used in the preparation of phenolic sulfones (50), but these compounds may also be prepared by a rearrangement of a sulfonate in the presence of aluminum chloride in a reaction similar to the Fries rearrangement (49):



A number of sulfones have been prepared by a combination of condensative and oxidative methods: an arenesulfonyl chloride is reacted with a *p*-substituted phenol and the resultant sulfide is oxidized to the sulfone (25):



A special class, the  $\alpha$ -disulfones, has been prepared by oxidation of sulfinic acids (*q.v.*):



**Sulfonation.** Sulfones may frequently be prepared by the action of sulfuric acid, sulfur trioxide, oleum, or chlorosulfonic acid on an aromatic hydrocarbon, or they may be prepared by an analogous reaction of a sulfonic acid with an aromatic hydrocarbon. Regardless of reagent, anhydrous conditions are necessary, and even under such circumstances sulfonation is difficult if the aromatic nucleus contains nitro or similar deactivating groups.

**Miscellaneous Methods.** As previously observed, the presence of a sulfonyl group in the alpha position of a carboxylic acid permits easy decarboxylation. Inasmuch as such acids are readily prepared, it is seen that this method affords a convenient source of a variety of sulfones.

A few sulfones have been prepared by addition reactions; hydroxy sulfones have been prepared by the addition of sulfinic acids to aldehydes and quinones. The formation of the thiacyclo-3-pentene 1,1-dioxides from conjugated diolefins and sulfur dioxide has already been described.

In many instances, a sulfone may be converted to a related sulfone by the ordinary reactions of organic chemistry. Thus a nitro sulfone may be converted to an amino sulfone by reduction, an amino sulfone may be diazotized to yield a phenolic sulfone, a methoxyaryl sulfone may be demethylated to yield a phenolic sulfone, etc. The addition of sulfinic acids to  $\alpha,\beta$ -unsaturated ketones and esters has been noted under *Sulfinic acids* (see p. 310).

### Uses

Sulfonal and related sulfones are used as hypnotics (see Vol. 7, p. 773). A few sulfones have been suggested as chemotherapeutic agents for the treatment of leprosy, tuberculosis, and pneumonia, but thus far they have been employed with conspicuous (although incomplete) success only in the treatment of leprosy (16). The compounds most commonly used for this purpose are bis(*p*-aminophenyl) sulfone (DDS); *p,p'*-diaminodiphenyl sulfone disodium formaldehydesulfoxylate (disodium [sulfonylbis-(*p*-phenylenimino)]dimethanesulfinate, sulfoxone sodium, N. N. R., Diasone Sodium),  $(C_6H_4NHCH_2SO_2Na)_2SO_2$ ; *p,p'*-diaminodiphenyl sulfone disodium *N,N'*-diglucosesulfonate (Promin),  $(CH_2OH(CHOH)_4CH(SO_2Na)NHC_6H_4)_2SO_2$ ; 4-aminophenyl 2-amino-5-thiazolyl sulfone (2-amino-5-sulfanilylthiazole, Promizole),  $NH_2C_6H_4SO_2-C:CH.N:C(NH_2).S$ ; and 4,4'-bis( $\gamma$ -phenylpropylamino)diphenyl sulfone tetrasodium sulfonate (Sulphetrone),  $(C_6H_5CH(SO_3Na)CH_2CH(SO_3Na)NHC_6H_4)_2SO_2$ . With the exception of Promizole, all the compounds listed are derivatives of DDS.

All these compounds listed have shown toxicity in varying degree and the following symptoms have been noted: normocytic anemia, methemoglobinemia, hematuria, leucopenia, drug rash, and nausea.

Numerous patents have been issued for the industrial utilization of sulfones. One such use, the reversible formation of sulfones from sulfur dioxide and conjugated dienes, has already been noted (56-61). The solvent action of liquefied sulfones has also been employed in the isolation of sulfur dioxide (54).

Addition of sulfones to Diesel fuels is claimed to cause an increase in cetane number (although less effectively than sulfoxides) and a decrease in pour point (63,64).

The chlorinated terpene sulfones containing at least 40% chlorine and the *N*-acyl derivatives of 3-aminothiacyclopentane 1,1-dioxide have shown insecticidal properties (62,66). The latter have also been patented as plasticizers and as ingredients in coating compositions and lube oils. Polymeric compounds have been represented as heat-resistant and permanently thermoplastic (67) and as useful in the production of adhesives and fibers (65).

The reaction products of bis(*p*-hydroxyphenyl) sulfone and such substances as glycolic acid, formaldehyde, and urea-formaldehyde mixtures have been patented as resins (48) or tanning agents (46,47,52,53). Certain nitro sulfones have been patented as dye intermediates (51).

The ethyl ester of sulfonyldiacetic acid has been recommended as a reagent in the identification of low-molecular-weight primary amines (1).



## Bibliography

- (1) Alden, J. P., and Houston, B., *J. Am. Chem. Soc.*, **56**, 413 (1934).
- (2) Amstutz, E. D., Hunsberger, I. M., and Chessick, J. J., *J. Am. Chem. Soc.*, **73**, 1220 (1951).
- (3) Barnard, D., Fabian, J. M., and Koch, H. P., *J. Chem. Soc.*, **1949**, 2442.
- (4) Bordwell, F. G., and Cooper, G. D., *J. Am. Chem. Soc.*, **74**, 1058 (1952).
- (5) Bordwell, F. G., and McKellin, W. H., *J. Am. Chem. Soc.*, **72**, 1985 (1950).
- (6) Bordwell, F. G., and McKellin, W. H., *J. Am. Chem. Soc.*, **73**, 2251 (1951).
- (7) Bradley, W., *J. Chem. Soc.*, **1938**, 458.
- (8) Cashmore, A. E., *J. Chem. Soc.*, **123**, 1738 (1923).
- (9) Cashmore, A. E., and McCombie, H., *J. Chem. Soc.*, **123**, 2884 (1923).
- (10) Djerassi, C., and Engle, R. R., *J. Am. Chem. Soc.*, **75**, 3838 (1953).
- (11) Fehnel, E. A., and Carmack, M., *J. Am. Chem. Soc.*, **72**, 1292 (1950).
- (12) Fenton, G. W., and Ingold, C. K., *J. Chem. Soc.*, **1930**, 705.
- (13) Field, L., *J. Am. Chem. Soc.*, **74**, 3919 (1952).
- (14) Galbraith, F., and Smiles, S., *J. Chem. Soc.*, **1935**, 1234.
- (15) Hinsberg, O., *Ber.*, **48**, 1611 (1915).
- (16) Johansen, F. A., and Erickson, P. T., *J. Am. Med. Assoc.*, **144**, 985 (1950).
- (17) Kent, B. A., and Smiles, S., *J. Chem. Soc.*, **1934**, 422.
- (18) Kliger, S. M., *J. Gen. Chem. (U.S.S.R.)*, **3**, 904 (1933); *C.A.*, **28**, 3051.
- (19) Koch, H. P., *J. Chem. Soc.*, **1949**, 408.
- (20) Koch, H. P., and Moffitt, W. E., *Trans. Faraday Soc.*, **47**, 7 (1951).
- (21) Kohler, E. P., and Potter, H. A., *J. Am. Chem. Soc.*, **57**, 1316 (1935).
- (22) Leonard, N. J., and Sutton, L. E., *J. Am. Chem. Soc.*, **70**, 1564 (1948).
- (23) Lewin, L. N., *J. Prakt. Chem.*, [2] **127**, 77 (1930).
- (24) Lister, M. W., and Sutton, L. E., *Trans. Faraday Soc.*, **35**, 495 (1939).
- (25) McClement, C. S., and Smiles, S., *J. Chem. Soc.*, **1937**, 1016.
- (26) Mellander, A. M., *Svensk. Kem. Tid.*, **46**, 99 (1934); *C.A.*, **28**, 5408.
- (27) Moffitt, W. E., *Proc. Roy. Soc. London*, **A200**, 409 (1950).
- (28) Overberger, C. G., Ligthelm, S. P., and Swire, E. A., *J. Am. Chem. Soc.*, **72**, 2856 (1950).
- (29) Phillips, G. M., Hunter, J. S., and Sutton, L. E., *J. Chem. Soc.*, **1945**, 146.
- (30) Price, C. C., and Gilbert, R. D., *J. Am. Chem. Soc.*, **74**, 2073 (1952).
- (31) Price, C. C., and Gillis, R. G., *J. Am. Chem. Soc.*, **75**, 4750 (1953).
- (32) Price, C. C., and Hydock, J. J., *J. Am. Chem. Soc.*, **74**, 1943 (1952).
- (33) Price, C. C., and Zomlefer, J., *J. Am. Chem. Soc.*, **72**, 14 (1950).
- (34) Schneider, W., *Ann.*, **386**, 343 (1912).
- (35) Schreiber, K. C., *Anal. Chem.*, **21**, 1168 (1949).
- (36) Shriner, R. L., Struck, H. C., and Jorison, W. J., *J. Am. Chem. Soc.*, **52**, 2068 (1930).
- (36a) Sugden, S.S., *The Parachor and Valency*, George Routledge and Sons, London, 1930, p.120.
- (37) Suter, C. M., *The Organic Chemistry of Sulfur*, Wiley, N.Y., 1944, ch. VII.
- (38) Todd, H. R., and Shriner, R. L., *J. Am. Chem. Soc.*, **56**, 1382 (1934).
- (39) Toussaint, J., *Bull. Soc. Chim. Belg.*, **54**, 319 (1945).
- (40) Vogel, A. I., *J. Chem. Soc.*, **1948**, 1833.
- (41) Vogel, A. I., Cresswell, W. T., Jeffery, G. H., and Leicester, J., *J. Chem. Soc.*, **1952**, 514.
- (42) Waldron, W. R., and Reid, E. E., *J. Am. Chem. Soc.*, **45**, 2411 (1923).
- (43) Warren, L. A., and Smiles, S., *J. Chem. Soc.*, **1930**, 1327.
- (44) Warren, L. A., and Smiles, S., *J. Chem. Soc.*, **1932**, 2774.
- (45) Ziegler, W. M., and Conner, R., *J. Am. Chem. Soc.*, **62**, 2596 (1940).
- (46) Brit. Pat. 504,994 (May 3, 1939), J. R. Geigy A.-G and R. M. Hughes.
- (47) Brit. Pat. 595,211 (Nov. 28, 1947), J. R. Geigy A.-G.
- (48) French Pat. 819,370 (Oct. 15, 1937), J. R. Geigy A.-G.
- (49) Ger. Pat. 532,403 (Jan. 9, 1930), K. W. Rittler (to Chemische Fabrik von Heyden A.-G.).
- (50) Ger. Pat. 555,409 (March 7, 1931), K. W. Rittler.
- (51) U.S. Pat. 1,939,416 (Dec. 12, 1933) K. Schimmelschmidt and H. Thomae (to General Aniline Works).
- (52) U.S. Pat. 2,174,287 (Sept. 26, 1939), F. W. Guthke (to I. G. Farbenind.).
- (53) U.S. Pat. 2,179,800 (Nov. 14, 1939), H. Schuette (to I. G. Farbenind.).
- (54) U.S. Pat. 2,368,545 (Jan. 30, 1945), G. W. Hooker, L. R. Drake, and S. C. Stowe (to Dow Chemical Co.).

- (55) U.S. Pat. 2,371,642 (March 20, 1945), R. Mozingo (to Merek and Co.).  
 (56) U.S. Pat. 2,373,563 (April 10, 1945), G. W. Hooker and S. C. Stowe (to Dow Chemical Co.).  
 (57) U.S. Pat. 2,380,832 (July 31, 1945), F. E. Frey and H. J. Hepp (to Phillips Petroleum Co.).  
 (58) U.S. Pat. 2,384,376 (Sept. 4, 1945), G. M. Hebbard (to Dow Chemical Co.).  
 (59) U.S. Pat. 2,399,837 (May 7, 1946), J. D. Upham (to Phillips Petroleum Co.).  
 (60) U.S. Pat. 2,402,891 (June 25, 1946), G. W. Hooker, L. R. Drake, and S. C. Stowe (to Dow Chemical Co.).  
 (61) U.S. Pat. 2,407,825 (Sept. 17, 1946), F. E. Frey and R. D. Snow (to Phillips Petroleum Co.).  
 (62) U.S. Pat. 2,435,071 (Jan. 27, 1948), T. W. Evans, R. C. Morris, and E. C. Shokal (to Shell Development Co.).  
 (63) U.S. Pat. 2,483,499 (Oct. 4, 1949), E. Lieber and A. F. Cashman (to Standard Oil Development Co.).  
 (64) U.S. Pat. 2,493,284 (Jan. 3, 1950), A. Farkas (to Union Oil Co. of California).  
 (65) U.S. Pat. 2,493,364 (Jan. 3, 1950), D. L. Schoene (to U.S. Rubber Co.).  
 (66) U.S. Pat. 2,514,564 (July 11, 1950), G. A. Buntin (to Hercules Powder Co.).  
 (67) U.S. Pat. 2,538,100 (Jan. 16, 1951), E. P. Irany and E. F. Landau (to Celanese Corp. of America).

E. G. RIETZ

**SULFONETHYLMETHANE**,  $C_2H_5(CH_3)C(SO_2C_2H_5)_2$ . See *Hypnotics and sedatives*, Vol. 7, p. 773.

## SULFONIC ACIDS

Sulfonic acids are characterized by the sulfo group,  $-SO_3H$  (or  $-SO_2OH$ ), and may be considered derivatives of sulfuric acid with one of the hydroxyl groups replaced by either an inorganic anion or a univalent organic radical.


The inorganic sulfonic acids have the general type formula  $XSO_3H$ , where X is commonly Cl, F, or  $NH_2$ . These compounds are discussed individually elsewhere (see *Chlorosulfonic acid*; *Fluorine compounds, inorganic*, Vol. 6, p. 734; *Sulfamic acid*). For the organic *N*-sulfonic acids see *Sulfamic acid*; *Sweetening agents*.

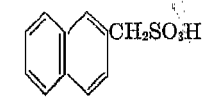
The organic sulfonic acids have the general type formula  $RSO_3H$  and are classified as alkanesulfonic acids, arenesulfonic acids, or heterocyclic sulfonic acids. The nature of the R group largely determines the physical and chemical properties of the individual acids, but, in general, they are nonoxidizing, water-soluble, stable acids comparable in strength to sulfuric acid. Careful distinction should be made between the sulfonic acids,  $RSO_2OH$ , and the sulfuric acid esters,  $ROSO_2OH$ , which are different in physical and chemical properties. See *Sulfuric and sulfurous esters*.

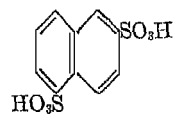
The alkane- and arenesulfonic acids and their derivatives are important industrial chemicals, useful as catalysts, detergents, emulsifying agents, and lubricating-oil additives. They are intermediates in the preparation of phenolic compounds, dyes, pharmaceuticals, and many other organic compounds. The preparation, properties, and uses of sulfonic acids and their derivatives are discussed by Gilman (1) and Suter (4).

**Nomenclature.** Sulfonic acids are named by adding this term as a suffix to the name of the parent hydrocarbon. When the hydrocarbon is of complex structure, additive names are often used. Examples are:

$CH_3SO_3H$   
Methanesulfonic  
acid

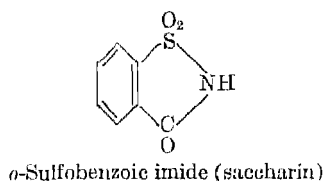
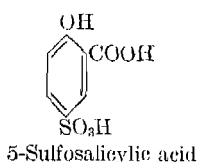
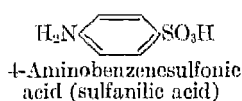
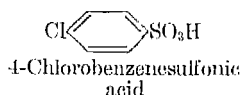
  
*p*-Toluene-  
sulfonic acid

  
2-Naphthalene-  
methanesulfonic acid

  
1,6-Naphthalene-  
disulfonic acid

The salts of alkyl-substituted arenesulfonic acids (used as surface-active agents) are commonly called "alkyl aryl sulfonates," but are better called alkylarenesulfonates by analogy with the names of specific members of the class, for example, sodium dodecylbenzenesulfonate.

Compounds containing other functional groups besides the  $-\text{SO}_3\text{H}$  group are named as derivatives of sulfonic acids. The only exceptions occur when the compound is also an -onium compound, an arsonic acid, or a carboxylic acid or derivative; in these cases the  $-\text{SO}_3\text{H}$  group is indicated by the prefix "sulfo-." Examples are:



Where common or trivial names have gained wide acceptance, they are preferred over the less familiar systematic ones. Thus the preferred name for 4-aminobenzenesulfonic acid is sulfanilic acid (see Vol. I, p. 923).

### Physical Properties

Like sulfuric acid, the organic sulfonic acids are hygroscopic, highly acidic, and water-soluble. Because of the influence of the organic radical, sulfonic acids may differ markedly from sulfuric acid in other physical properties such as solubility in organic solvents.

In the aliphatic series, methanesulfonic acid is a crystalline solid melting at  $20^\circ\text{C}$ . Homologs from ethanesulfonic acid through *n*-hexanesulfonic acid are oily liquids at room temperature. Higher members are usually low-melting crystalline solids (see Table I). All the acids are difficult to obtain in anhydrous form. The lower members of the series are completely miscible with water at room temperature. However, as molecular weight increases, water solubility decreases; *n*-hexadecanesulfonic acid is only slightly soluble at room temperature.

TABLE I. Physical Properties of Some Alkanesulfonic Acids.

Sulfonic acid	B.p., 1 mm., $^\circ\text{C}$ .	M.p., $^\circ\text{C}$ .	$d_4^{25}$
Methane-	122	20	1.4844
Ethane-	123	-17	1.3341
Propane-	136	7.5	1.2516
Butane-	149	-15.2	1.1906
Pentane-	163	15.9	1.1226
Hexane-	174	16.1	1.1047
Hexadecane-	—	53	—
2-Aminoethane- (taurine)	—	305-10 (dec)	—

Arenesulfonic acids are generally solids at room temperature. They crystallize from water as low-melting, colorless, deliquescent hydrates. It is difficult to prepare

the free acids in anhydrous form, and for this reason there is little agreement in the literature on their physical properties. For example, melting points ranging from 52 to 66°C. are reported for the simplest member of the series, benzenesulfonic acid, and the range is even larger for many others. The free acids have very high boiling points and usually decompose on distillation.

Detailed descriptions of the more important acids are given elsewhere. See *Benzenesulfonic acid*; *Naphthalenesulfonic acids*; *p-Toluenesulfonic acids*. See also "Sulfonic acid derivatives" under *Aniline*; *Amino naphthols and aminonaphtholsulfonic acids*; *Anthraquinone derivatives*; *Naphthols and naphtholsulfonic acids*; *Naphthylamines and naphthylaminesulfonic acids*; *Phenolsulfonic acids*; "Sulfosalicylic acid," Vol. 12, p. 59.

### Chemical Properties

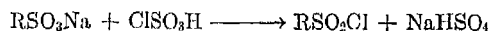
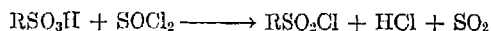
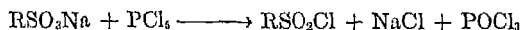
The sulfonic acids are almost completely ionized in aqueous solution and in solutions of many polar organic solvents. They are comparable in acid strength to sulfuric acid. The chemical reactions of the sulfonic acids can be divided into four categories on the basis of structural changes that occur.

**Salt formation** occurs when the hydrogen atom of the sulfonic acid group is replaced by reaction of the acid with metals above hydrogen in the electromotive series. Metal salts are also formed by reaction with inorganic oxides, hydroxides, and carbonates. With ammonia and its derivatives, ammonium and substituted ammonium salts are formed. In most cases, the salts are crystalline solids that are much more water-soluble than the corresponding sulfates (see Table II). Some amine salts, such as triethylammonium ethanesulfonate, are mobile liquids at room temperature.

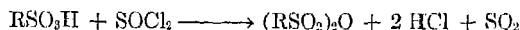
TABLE II. Water Solubility of Sulfonates and Sulfates in g./100 g. H<sub>2</sub>O at 20°C.

Cation	Methanesulfonate	Ethanesulfonate	Sulfate
NH <sub>4</sub> <sup>+</sup>	145	252	75
Ba <sup>2+</sup>	70	73	2 × 10 <sup>-6</sup>
Ca <sup>2+</sup>	—	87	3 × 10 <sup>-1</sup>
Co <sup>2+</sup>	75	83	36
Cu <sup>2+</sup>	68	90	21
Pb <sup>2+</sup>	143	175	4 × 10 <sup>-4</sup>
Li <sup>+</sup>	142	210	35
Mg <sup>2+</sup>	—	40	34
K <sup>+</sup>	106	141	11
Na <sup>+</sup>	100	105	19
Ag <sup>+</sup>	101	—	8 × 10 <sup>-1</sup>
Zn <sup>2+</sup>	76	76	116

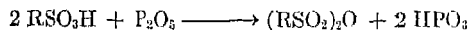
**Replacement of the hydroxyl** of the sulfonic acid group by chlorine is accomplished by reaction of the sulfonic acid or its salt with phosphorus pentachloride, thionyl chloride, or chlorosulfonic acid to give sulfonyl chlorides:



Similarly, sulfonyl bromides can be prepared with phosphorus pentabromide or thionyl bromide, and sulfonyl fluorides with fluorosulfonic acid. Unless these reactions are carefully controlled, sulfonic acid anhydrides may occur as by-products. In fact, the reaction of thionyl chloride with sulfonic acids can be carried out to yield *sulfonic anhydrides* as the principal product:



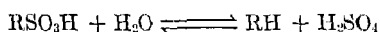
Anhydrides can also be made by the dehydration of sulfonic acids with dehydrating agents such as phosphorus pentoxide:



Preparation of only the lower anhydrides by these methods has been worked out.

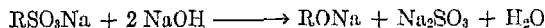
**Acid or alkaline hydrolysis** in which the entire sulfonic acid group is replaced by a hydrogen or hydroxyl group illustrates the effect of the structure of the hydrocarbon portion of the molecule upon chemical reactivity of the acids. Ordinarily, the sulfonic acids are very stable, but the C—S bond can be broken if sufficiently drastic conditions are used.

Since sulfonation of a hydrocarbon is a reversible reaction, heating a sulfonic acid with water or mineral acids should give sulfuric acid and the original unsulfonated compound:



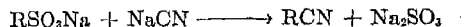
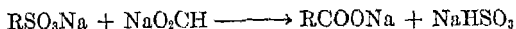
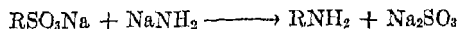
Alkanesulfonic acids are not hydrolyzed by water or mineral acids even at high temperatures. With arenesulfonic acids the ease of hydrolysis of the acid varies widely with the nature of the hydrocarbon group. In the presence of mineral acids, benzenesulfonic acid is difficult to hydrolyze, whereas some more highly substituted benzenesulfonic acids hydrolyze readily. Steam at 160°C. will hydrolyze 1-naphthalenesulfonic acid but not 2-naphthalenesulfonic acid; the difference in ease of hydrolysis has been used commercially to separate these isomers.

Alkaline fusion or hydrolysis of sulfonic acids, in contrast to the acidic hydrolysis to yield hydrocarbons, results in replacement of the sulfonic acid group by the hydroxyl group:



Alkanesulfonic acids resist hydrolysis; boiling dilute sodium hydroxide has no effect. More concentrated alkali at high temperatures results in a slow reaction, but any alcohol formed is oxidized to other products. In the aromatic series, alkaline hydrolysis is a widely used reaction; high yields of phenolic compounds are obtained commercially by fusion of sulfonic acid salts with alkali at high temperatures. See *Naphthols*; *Phenol and phenols*, Vol. 10, pp. 286, 309; *Resorcinol*, Vol. 11, p. 714.

Salts of arenesulfonic acids react with sodamide, sodium or potassium formate, and sodium cyanide to give amines (*q.v.*), carboxylic acids (*q.v.*), and nitriles (*q.v.*), respectively:



The yields in these reactions are usually poor.

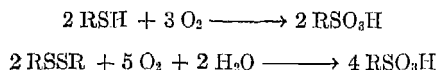
**Substitutions of the hydrocarbon portion** of the sulfonic acid molecule are confined

primarily to the arenesulfonic acids, since at least the lower alkanesulfonic acids are unaffected by concentrated nitric acid, oleum, or halogens. Arenesulfonic acids react in several ways. When only ring substitution occurs, the sulfonic acid group is generally stated to be meta-directing. However, isomers other than meta are formed in yields that depend upon the nature of the sulfonic acid and the reagent. For example, benzenesulfonic acid with bromine and water gives chiefly *m*-bromobenzenesulfonic acid, whereas nitration gives a mixture of *o*-, *m*-, and *p*-nitrobenzenesulfonic acids (see Vol. 2, p. 443). These reagents may also replace the sulfonic acid group under appropriate conditions; for example, *p*-xylenesulfonic acid reacts with an excess of bromine water to give 2,5-dibromo-*p*-xylene.

### Preparation

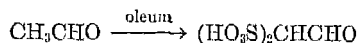
Different methods are used commercially to prepare alkanesulfonic acids and arenesulfonic acids. The inertness of alkanes demands indirect methods, whereas the high reactivity of arenes permits direct introduction of the sulfonic acid group.

**Alkanesulfonic acids** are made by the oxidation of mercaptans or disulfides (see also Vol. 8, p. 862; Vol. 13, p. 300):

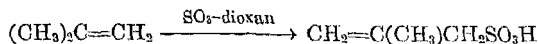


Direct sulfonation of hydrocarbons can be used, but the yields are poor and the method is not practical. (See also Vol. 6, p. 220.) The commercially available alkanesulfonic acids of low molecular weight are prepared by oxidation of alkyl disulfides (5,6,8) or mercaptans (9) with air or oxygen in the presence of nitric acid or nitrogen oxide catalysts. The alkyl disulfides or mercaptans are usually obtained as by-products in petroleum refining (see Vol. 10, p. 143). The acid is freed of catalyst and any excess water after oxidation is complete. The process can be operated under anhydrous conditions to produce the sulfonic acid anhydride (7).

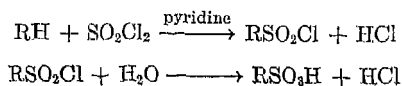
Direct sulfonation of paraffinic or olefinic aldehydes, ketones, and acids yields sulfonic acid derivatives of these oxygenated compounds. For example, acetaldehyde can be sulfonated to introduce two sulfonic acid groups:



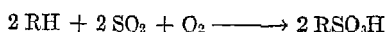
Sulfur trioxide addition compounds are useful for the direct sulfonation of olefins or their derivatives. For example, isobutylene can be sulfonated with the sulfur trioxide-dioxan addition compound:



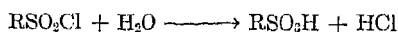
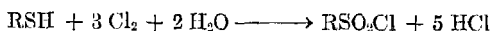
Two other methods for the preparation of aliphatic sulfonic acids are based on the reactions of hydrocarbons with sulfuryl chloride (or sulfur dioxide plus chlorine) and with sulfur dioxide and oxygen. The reaction with sulfuryl chloride is carried out in the presence of a weak base, such as pyridine, to yield sulfonyl chlorides (see p. 412). These can be readily hydrolyzed to sulfonic acids:



The reaction of hydrocarbons with sulfur dioxide and oxygen gives sulfonic acids directly:



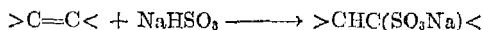
A convenient laboratory method for the preparation of sulfonic acids is based on the chlorination of mercaptans to yield sulfonyl chlorides, which can be readily hydrolyzed to the sulfonic acids:



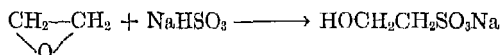
Salts of alkanesulfonic acids can be prepared by the action of metallic sulfites on organic halides:



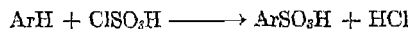
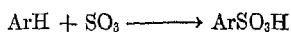
and by the addition of sodium bisulfite to olefins:



Salts of sulfonic acids can also be prepared by the reaction of epoxides with sodium bisulfite. For example, ethylene oxide reacts with sodium bisulfite to give the sodium salt of isethionic acid:



**Arenesulfonic acids** are made by the direct sulfonation of hydrocarbons with sulfuric acid, sulfur trioxide, oleum, or chlorosulfonic acid:



The direct sulfonation technique is used to prepare individual sulfonic acids. (See Vol. 2, p. 443; Vol. 9, p. 233; *Naphthalenesulfonic acids*; *Toluenesulfonic acids*.) It is also applied to hydrocarbon mixtures in petroleum refining to yield by-product acids, the chemical nature of which is not clear. They are mainly aromatic and are usually converted to salts and sold as oil-salt mixtures. See also *Petroleum chemicals*, Vol. 10, pp. 202, 209; *Sulfonation and sulfation*.

The principal commercially available sulfonic acids are benzenesulfonic acid, toluenesulfonic acid, dodecylbenzenesulfonic acid, and mixed alkanesulfonic acids—a mixture of methane-, ethane-, and propanesulfonic acids. The alkanesulfonic acid mixture is available as a liquid containing 92–95% sulfonic acid, 1–2% sulfuric acid, and 3–6% water. It is shipped in glass carboys. Dodecylbenzenesulfonic acid, sold as 95–96% acid, is available in tank car lots. It is shipped in stainless steel containers or containers lined with Heresite (phenol-formaldehyde type resin).

Construction materials for handling sulfonic acids vary greatly with the concentration, temperature, and sulfuric acid content. Stainless steel is generally recommended; it resists attack, even at elevated temperatures.

### Toxicity

The toxicological properties of sulfonic acids as a group have been little investigated, but the toxicity of individual sulfonic acids probably depends largely upon the

structure of the parent hydrocarbon. Toxicological work with animals has shown that the lower alkanesulfonic acids are not unusually hazardous. When given orally in dilute solution to rabbits, the free acids are about as toxic as hydrochloric acid, and the sodium salts are no more toxic than most alkali metal salts of strong acids. However, as strong acids, the sulfonic acids and concentrated aqueous solutions of them cause burns of the skin and mucous membranes and should be handled accordingly.

### Uses

Sulfonic acids are among the most important industrial chemicals. The free acids are used in smaller volumes than their salts, but both are highly useful as reaction intermediates.

The primary uses of free sulfonic acids are as catalysts in many organic reactions. Their strongly acidic nature and nonoxidizing properties make them useful as catalysts for such reactions as esterification, polymerization, hydrolysis, and alkylation. These applications represent the major use of the alkanesulfonic acids (2,3) but consume only a minor part of the commercially produced arenesulfonic acids.

The arenesulfonic acids and their salts are used in making many chemical compounds. The caustic hydrolysis of sulfonic acids such as benzenesulfonic acid and *m*-benzenedisulfonic acid is a general method for the preparation of phenolic compounds, the most important of which is phenol (*q.v.*). Various aromatic sulfonic acids are important dye intermediates. Sulfonate dyes, although marketed as salts, are applied to fabrics in acid baths and therefore are, in effect, used in the acid form. This market consumes a large amount of sulfonic acid derivatives. Similarly, sulfonic acid ion-exchange resins exist in the acid form during part of their normal use cycle, and in the acid form they are also effective catalysts.

Many sulfonic acid salts possess surface-active properties. The recent growth of synthetic detergents has made dodecylbenzenesulfonates the largest single outlet for sulfonic acids. Fatty acid esters of 2-hydroxyethanesulfonic acid (isethionic acid), such as Igepon A, and fatty acid amides of 2-aminoethanesulfonic acid (taurine), such as Igepon T, were among the first surface-active agents (*q.v.*) introduced. By-product petroleum sulfonates are widely used as emulsifying agents, rust inhibitors, and lubricating-oil additives, and as ingredients of soluble oils. Sulfonated fatty acids and oils have long been used in the textile, leather, paper, and glue industries.

### Derivatives

Aside from the salts, important derivatives of sulfonic acids include sulfonyl halides, sulfonamides, and esters. The **sulfonyl halides**,  $\text{RSO}_2\text{X}$ , ranging from mobile liquids to crystalline solids, are extremely reactive. They are therefore useful in the preparation of many sulfonic acid derivatives. Sulfonyl chlorides react with ammonia and amines to form sulfonamides (*q.v.*; see also *Chloramines*, Vol. 3, p. 760; *Sulfa drugs*; "Saccharin" under *Sweetening agents*). A wide variety of sulfonamides is used in pharmaceutical preparations. The sulfonyl chlorides react with alcohols to yield **esters** of sulfonic acids. The esters are highly reactive and are used to alkylate amines, alcohols, and hydrocarbons. (See *Toluenesulfonic acids*.) Certain esters can also be prepared by the reaction of sulfonic acids with olefins. Intramolecular esters of hydroxy sulfonic acids are called *sultones*, and intermolecular esters are called *sulfonylides*. Intramolecular condensation products from amino sulfonic acids are called



*sultams*. Condensation products of *o*-sulfobenzoic anhydrides and phenolic compounds are known as *sulfonephthaleins*. (See *Sulfur compounds, organic*.) Sulfonyl chlorides can be reduced by means of zinc dust in water to yield sulfinic acids (*q.v.*),  $\text{RSO}_2\text{H}$ , or with zinc dust and aqueous mineral acid to yield mercaptans (*q.v.*),  $\text{RSH}$ .

### Bibliography

- (1) Gilman, H., *Organic Chemistry, An Advanced Treatise*, Wiley, N.Y., 1944.
- (2) Proell, W. A., and Adams, C. E., *Ind. Eng. Chem.*, **41**, 2217 (1949).
- (3) Proell, W. A., Adams, C. E., and Shoemaker, B. H., *Ind. Eng. Chem.*, **40**, 1129 (1948).
- (4) Suter, C. M., *The Organic Chemistry of Sulfur*, Wiley, N.Y., 1944, chs. II-V.
- (5) U.S. Pat. 2,433,395 (Dec. 30, 1947), W. A. Proell and B. H. Shoemaker (to Standard Oil Co. (Indiana)).
- (6) U.S. Pat. 2,437,396 (Dec. 30, 1947), W. A. Proell (to Standard Oil Co. (Indiana)).
- (7) U.S. Pat. 2,489,316 (Nov. 29, 1949), W. A. Proell (to Standard Oil Co. (Indiana)).
- (8) U.S. Pat. 2,489,318 (Nov. 29, 1949), W. A. Proell (to Standard Oil Co. (Indiana)).
- (9) U.S. Pat. 2,505,910 (May 2, 1950), W. A. Proell and B. H. Shoemaker (to Standard Oil Co. (Indiana)).

A. A. HARBAN AND C. E. JOHNSON

**SULFONIUM COMPOUNDS.** See *Onium compounds*; *Sulfides, organic*; *Sulfur compounds, organic*.

**SULFONMETHANE**,  $(\text{CH}_3)_2\text{C}(\text{SO}_2\text{C}_2\text{H}_5)_2$ . See *Hypnotics and sedatives*, Vol. 7, p. 773.

**SULFONYL HALIDES**,  $\text{RSO}_2\text{X}$ . See *Sulfonic acids*.

**SULFONYLIDES**. See *Sulfur compounds, organic*.

**5-SULFOSALICYLIC ACID**,  $(\text{OH})\text{C}_6\text{H}_3(\text{SO}_3\text{H})\text{COOH}$ . See *Salicylic acid*, Vol. 12, p. 59.

**SULFOXIDATION**. See *Sulfonation and sulfation*.

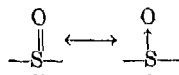
### SULFOXIDES

Sulfoxides,  $\text{R}_2\text{SO}$ , are characterized by the linkage of the sulfinyl group,  $-\text{SO}-$ , with two different carbon atoms. Sulfoxides are an intermediate oxidation stage between organic sulfides (*q.v.*) and sulfones (*q.v.*). Conceivably, disulfoxides structurally similar to the  $\alpha$ -disulfones could exist, but compounds once believed to be disulfoxides of the formula  $\text{R}-\text{SO}-\text{SO}-\text{R}$  have been shown to be esters of thiolsulfonic acids,  $\text{R}-\text{SO}_2-\text{S}-\text{R}$  (9). However, numerous disulfoxides with isolated sulfinyl groups are known. Cyclic sulfoxides are also known.

Relatively few sulfoxides occur in nature, but two optically active sulfoxides, sulforaphen (4-(methylsulfinyl)-3-butenyl isothiocyanate) and 4-(methylsulfinyl)-3-butenyl cyanide, have been found as glucosides in radish seed (19), and alliin (*S*-allyl-cysteine sulfoxide) has been observed in certain garlies (25).

Although sulfoxides resemble ketones superficially in formula, with sulfur in place of carbon, the two classes of compounds are dissimilar in properties. The recognition of optical isomerism in sulfoxides containing two different radicals linked to the sulfinyl group (such as *p*-tolyl *p*-aminophenyl sulfoxide) and the successful resolution of such compounds in 1928 (10), as well as studies of the parachor (26), indicated a marked difference between sulfoxides and ketones. Recently Karrer and co-workers have extended the stereochemistry of the sulfoxides by the assignment

of D- and L- configurations to simple members (12). Sulfoxides are now known to have a pyramidal structure, and the sulfur-oxygen bond, like that in sulfones, is thought to be a resonance hybrid between a double bond and a semipolar bond (31):



See also *Stereochemistry (organic)*, Vol. 12, p. 861; *Sulfur compounds—structure*.

Sulfoxides are commonly named like ethers or sulfides by means of hydrocarbon radicals, for example  $(\text{C}_6\text{H}_5)_2\text{SO}$ , phenyl sulfoxide or diphenyl sulfoxide. The I.U.P.A.C. system names them as substitution products, as *o*- $\text{NH}_2\text{C}_6\text{H}_4\text{SOC}_6\text{H}_5$ , *o*-(phenylsulfinyl)aniline. The prefix sulfinyl (also sometimes called thionyl or sulfoxy) is also used for sulfoxides containing certain other functional groups, as  $\text{SO}(\text{CH}_2\text{COOH})_2$ , sulfinyl(or thionyl)diacetic acid;  $\text{C}_6\text{H}_5\text{SOCH}_2\text{COOH}$ , phenylsulfoxyacetic acid. Sulfoxides derived from cyclic or other complicated sulfides are often designated "oxides," for example, thiophene 1-oxide (or *S*-oxide).

### Properties

For the most part, sulfoxides are crystalline, colorless substances, although the lower aliphatic sulfoxides melt at relatively low temperatures (see Table I). The lower aliphatic sulfoxides are water-soluble, but as a class the sulfoxides are not soluble in water, although they are soluble in dilute acids, and a few are soluble in alkaline solution. They are soluble to a variable extent in organic solvents, depending upon associated functional groups. They are usually unstable toward heat and rarely may be distilled at atmospheric pressure; even vacuum distillation is often unsatisfactory.

TABLE I. Melting Points of Sulfoxides.

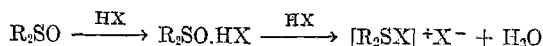
Formula	M.p., °C.	Formula	M.p., °C.
$(\text{CH}_3)_2\text{SO}$	8	$\text{C}_6\text{H}_5\text{SOCH}_2\text{COOH}$	116
$(\text{C}_2\text{H}_5)_2\text{SO}$	15	$\text{C}_6\text{H}_5\text{CH}_2\text{SOC}_6\text{H}_5$	125
$(n\text{-C}_3\text{H}_7)_2\text{SO}$	18	<i>p</i> - $\text{CH}_3\text{C}_6\text{H}_4\text{SOC}_6\text{H}_5$	124
$(n\text{-C}_4\text{H}_9)_2\text{SO}$	32	$(\text{C}_6\text{H}_5\text{CH}_2)_2\text{SO}$	135
$((\text{CH}_3)_2\text{CHCH}_2\text{CH}_2)_2\text{SO}$	39	$(2\text{-NO}_2\text{C}_6\text{H}_4)_2\text{SO}$	184
$(n\text{-C}_7\text{H}_{15})_2\text{SO}$	70	4,2-(BrNO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> ) <sub>2</sub> SO	238
$(\text{ClCH}_2\text{CH}_2)_2\text{SO}$	110	$\text{C}_6\text{H}_5\text{SOCH}_2\text{CH}_2\text{SOC}_2\text{H}_5$	170
$(\text{C}_2\text{H}_5\text{OCH}_2\text{CH}_2)_2\text{SO}$	b <sub>15</sub> 176–80	1,4-(C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> SOCH <sub>2</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	233

**Reactions.** Sulfoxides undergo reaction with oxidants, reductants, acids, and salts, and participate in condensations. They are differentiated in these reactions from their related compounds the sulfones.

Sulfoxides are readily oxidized to sulfones, which are stable and resist further oxidation. The oxidants listed under "Preparation" are capable of accomplishing this reaction. Reduction of sulfoxides readily yields sulfides and sometimes quantitatively with such diverse agents as zinc dust, the hydrogen halides (1), and sodium. Raney nickel differs from the reductants listed in that it effects desulfurization (3,38).

The sulfoxides are further differentiated from the sulfones by their greater reactivity with acids. Szmant and Brost (29) examined the cryoscopic behavior of sulfoxides in sulfuric acid and observed that a sulfoxidonium ion,  $\text{R}_2\text{SOH}^+$ , or a sulfidonium ion,  $\text{R}_2\text{S}^{2+}$ , may be formed. In general, sulfones are only partially proto-

nated under these conditions. In certain instances sulfoxides react with acids to form mono- and diacid salts:

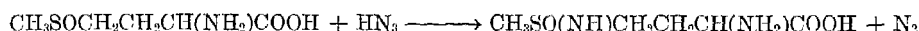


However, only a few salts of the above types have been isolated. The monoacid salts are represented by the nitrates of methyl sulfoxide, 1,2-bis(benzylsulfinyl)ethane, and the isomeric disulfoxides of dithiane. The diacid salts are represented by only a few halides. These compounds are identical with the dihalides obtained directly by the action of a halogen on a sulfide. In all probability the reduction of a sulfoxide by a hydrogen halide proceeds via the diacid salt:



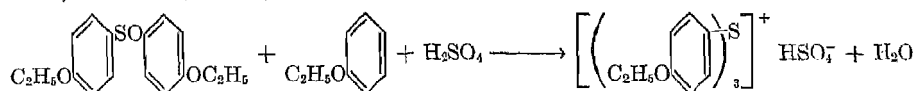
If the sulfoxide contains a readily substituted radical, the sulfide formed in the above sequence may be obtained in the form of its *C*-halogenated derivative.

Certain cyclic aromatic sulfoxides such as those of thiaxanthene and thianthrene react with acids to form quinoidal salts. The halides are identical with those formed by the action of the halogens on the sulfides. An unusual class of compounds, the *sulfoximines*, has recently been prepared by the action of hydrazoic acid on a sulfoxide. One such compound, methionine sulfoximine, has been synthesized and has been found to be identical with a toxic principle of "agenized" flour (5) (see also Vol. 3, p. 623):

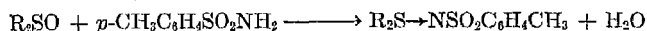


Sulfoxides also form well-defined crystalline complexes with a number of inorganic acids and salts. In this respect they resemble the sulfides and differ from the sulfones. Among the complexes recorded are those with mercuric chloride, ferric chloride, chloroplatinic acid, ferrocyanic acid, chlorauric acid, calcium nitrate, and calcium iodide. The composition of these compounds is variable, ranging from  $(C_2H_5)_2SO \cdot H_4Fe(CN)_6$  to  $((C_2H_5)_2SO)_5 \cdot H_2PtCl_6$ .

Sulfoxides undergo condensation reactions but, with the exception of a few ambiguous cases, these reactions differ from the condensations of the sulfones in that they do not occur at  $\alpha$ -methylene groups but proceed to the formation of sulfonium salts (24). In general, the condensations involve the reaction of aromatic sulfoxides with phenols, ethers of phenols, and aromatic amines to give sulfonium compounds:



Condensations of this type may cause significantly lowered yields of sulfoxides in their preparation from thionyl chloride or from sulfur dioxide. A somewhat different condensation has been observed between tetramethylene sulfoxide and sulfonamides or substituted acetamides to yield sulfilmines (sulfilmines) (30):

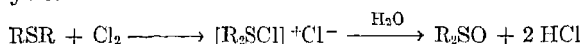


The low degree of activity of methylenic groups alpha to the sulfinyl indicates that the sulfinyl group does not exert an activating effect comparable to that of the carbonyl, and the typical reactions of enolization are not observed. Thus, bis(phenylsulfinyl)methane, a compound in which two sulfinyl groups may exert a concerted effect upon the methylene group, undergoes no alkylation with methyl iodide, is insoluble in dilute sodium carbonate solution, and gives no test with ferric chloride (21). A few sulfoxides are soluble in dilute alkali, but in all probability this behavior is a

result of the electrostatic effect accruing from the polar sulfinyl group, an effect analogous to that of an  $\alpha$ -halogen atom on the ionization constant of an aliphatic carboxylic acid. Studies of the copolymerization of methyl vinyl sulfoxide with styrene and methyl methacrylate indicate a low conjugative effect of the sulfinyl group (18).

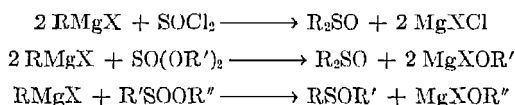
### Preparation

In general, sulfoxides are prepared by oxidation of sulfides, the proportion of oxidant and the temperature being adjusted to prevent excessive oxidation and consequent formation of a sulfone. In a few instances, anodic oxidation has been employed. Among the chemical oxidants used are nitric acid, hydrogen peroxide (8,28), chromic acid or dichromates, permanganate, organic peroxides (2,15), hypochlorite (17,33), oxides of nitrogen, air oxidation (4), and halogens. Oxidation with the halogens is normally accomplished in two steps: the formation of the sulfide dihalide and subsequent hydrolysis:



Of the agents listed, hydrogen peroxide is of greatest general usefulness.

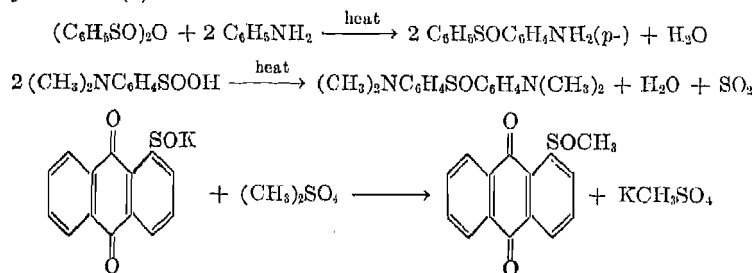
Two other preparative methods, the Grignard reaction and the Friedel-Crafts (or related) reaction, have found limited use. The four agents employed in the Grignard synthesis, thionyl chloride, alkyl sulfites (8), sulfinic esters (8), and sulfonyl chlorides (11), have been used with variable effectiveness but, except for the sulfites, side reactions are common:



The practicality of the Grignard synthesis indicates a low reactivity of sulfoxides toward the Grignard reagent. Under drastic conditions, however, a reaction is observed and a sulfonium salt is produced (32).

The Friedel-Crafts type of reaction has been used to a limited extent in the preparation of sulfoxides from the reaction of thionyl chloride (23) or sulfur dioxide with such aromatic compounds as hydrocarbons, phenols (22), ethers of phenols (23,24), and certain secondary amines (16). In some instances, the reaction proceeds to the formation of a triarylsulfonium salt of the type  $[\text{Ar}_3\text{S}]^+\text{Cl}^-$ .

Although most sulfoxides are prepared by the three methods listed, a few are prepared by miscellaneous methods such as the condensation of a sulfinic anhydride with aromatic compounds (13), the formation of sulfoxides directly from sulfinic acids by the loss of water and sulfur dioxide (16), and the reaction of alkali sulfenates with methyl sulfate (6):



## Uses

Relatively few uses have been proposed for the sulfoxides. Like the *p,p'*-diaminodiphenyl sulfones, the substituted diphenyl sulfoxides have given some indication of effectiveness against disease organisms (7,14,34), but widespread clinical use of the sulfoxides has not been reported. Patents have also been issued for the use of sulfoxides as dye intermediates (35,36) and as extracting agents (37).

## Bibliography

- (1) Bell, E. V., and Bennett, G. M., *J. Chem. Soc.*, **1927**, 1803.
- (2) Bohme, H., *Ber.*, **70**, 379 (1937).
- (3) Bonner, W. A., *J. Am. Chem. Soc.*, **74**, 5090 (1952).
- (4) Bougault, J., and Robin, P., *Compt. rend.*, **171**, 353 (1920); *J. Pharm. Chim.*, **23**, 49 (1921).
- (5) Challenger, F., *Endeavour*, **12**, 178 (1953).
- (6) Fries, K., *Ber.*, **45**, 2971 (1912).
- (7) Gerard, A., Ray, A., and Richard, G., *Nature*, **140**, 283 (1937).
- (8) Gilman, H., Robinson, J., and Beaber, N. J., *J. Am. Chem. Soc.*, **48**, 2717 (1926).
- (9) Gilman, H., Smith, L. E., and Parker, H. H., *J. Am. Chem. Soc.*, **47**, 851 (1925).
- (10) Harrison, P. W. B., Kenyon, J., and Phillips, H., *J. Chem. Soc.*, **1926**, 2079.
- (11) Hepworth, H., and Clapham, H. W., *J. Chem. Soc.*, **119**, 1188 (1921).
- (12) Karrer, P., Antia, N. J., and Schwyzer, R., *Helv. Chim. Acta*, **34**, 1392-99 (1951); *C.I.*, **46**, 4991.
- (13) Knoevenagel, E., and Polack, L., *Ber.*, **41**, 3323 (1908).
- (14) Levaditi, C., Girard, A., Vaisman, A., Ray, A., and Richard, G., *Compt. rend.*, **205**, 1018 (1937).
- (15) Lewin, L. N., *J. Prakt. Chem.*, **127**, 77 (1930).
- (16) Michaelis, A., and Schindler, P., *Ann.*, **310**, 148 (1900).
- (17) Muller, E., and Metzger, H., *J. Prakt. Chem.*, [2] **114**, 123 (1926).
- (18) Price, C. C., and Gilbert, R. D., *J. Am. Chem. Soc.*, **74**, 2073 (1952).
- (19) Schmid, H., and Karrer, P., *Helv. Chim. Acta*, **31**, 1017, 1087 (1948).
- (20) Scott, J. D., *Sulfoxides* (Master's Thesis), Univ. of Chicago, 1928.
- (21) Shriner, R. L., Struck, H. C., and Jorison, W. S., *J. Am. Chem. Soc.*, **52**, 2060 (1930).
- (22) Smiles, S. S., and Bain, A. W., *J. Chem. Soc.*, **91**, 1118 (1907).
- (23) Smiles, S. S., and LeRossignol, R., *J. Chem. Soc.*, **89**, 706 (1906).
- (24) Smiles, S. S., and LeRossignol, R., *J. Chem. Soc.*, **93**, 745 (1908).
- (25) Stoll, A., and Seebeck, E., *Experimentia*, **3**, 114 (1947).
- (26) Sugden, S. S., *The Parachor and Valency*, George Routledge and Sons, London, 1930, p. 120.
- (27) Suter, C. M., *The Organic Chemistry of Sulfur*, Wiley, N.Y., 1944, p. 660.
- (28) Sunthakar, A. V., Tilak, B. D., and Venkataraman, K., *Current Sci. (India)*, **20**, 155 (1951); *C.A.*, **46**, 11140.
- (29) Szmant, H. H., and Brost, G. A., *J. Am. Chem. Soc.*, **73**, 4175 (1951).
- (30) Tarbell, D. S., and Weaver, C., *J. Am. Chem. Soc.*, **63**, 2939 (1941).
- (31) Wheland, G. W., *Advanced Organic Chemistry*, Wiley, N.Y., 1949, pp. 356-60.
- (32) Wildi, B. S., Taylor, S. W., and Potratz, H. A., *J. Am. Chem. Soc.*, **73**, 1935 (1951).
- (33) Wood, A. E., and Travis, E. G., *J. Am. Chem. Soc.*, **50**, 1226 (1928).
- (34) Brit. Pat. 517457 (Jan. 30, 1940), S. Ellingworth and F. J. Rose (to Imperial Chem. Ltd.).
- (35) U.S. Pat. 2,140,569 (Dec. 20, 1938), H. Ufer and O. Hecht (to I. G. Farbenind.).
- (36) U.S. Pat. 2,163,180 (June 20, 1939), H. Ufer (to I. G. Farbenind.).
- (37) U.S. Pat. 2,365,898 (Dec. 26, 1944), R. C. Morris and N. C. Melchior (to Shell Development Co.).
- (38) U.S. Pat. 2,371,641 (March 20, 1945), R. Mozingo (to Merck & Co.).

E. G. RIETZ

**SULFOXIMINES, R<sub>2</sub>SO(NH).** See *Sulfoxides*, p. 355; *Sulfur compounds, organic*, p. 441.

## SULFUR

Sulfur, S, atomic weight 32.066, atomic number 16, is in Group VI, period 3, of the periodic table. The name is believed to be derived from the Sanskrit *klubere* through the Latin *sulfurium* or *sulfurum*. Although the A.C.S. approved spelling is sulfur, the spelling sulphur is frequently used commercially. It is also often called brimstone, and this name occurs in the Bible. See also *Sulfur compounds, inorganic*; *Sulfur compounds, organic*; *Sulfuric acid*.

Whereas sulfur has been known for thousands of years, it was considered a strange earth until Lavoisier demonstrated that it is an elementary substance.

Historians report that some 20 centuries before the birth of Christ sulfur was used by priests in religious ceremonies. Its bright, ethereal blue flame and pungent odor gave added mysticism to temple sacrifices and purification rites. From the practical standpoint, sulfur began to be put to more and more useful purposes around 1600 B.C. Sulfur dioxide prepared by burning sulfur was found to be an excellent and efficient bleaching agent for cotton and linen, and it is known that the Egyptian artists around this time were using colors containing sulfur compounds. Sulfur has been referred to in classical literature. Homer tells how Odysseus, after slaying the suitors for his wife's hand, cleaned and purified his house by burning sulfur. During the time of Confucius, the Chinese invented gunpowder, using sulfur as an ingredient. Pliny, writing around A.D. 50 told of four kinds of sulfur having 14 medicinal virtues.

The first commercial sulfur in modern times was produced in Sicily early in the 15th century. But it was not until 1735, when a process for the manufacture of sulfuric acid from sulfur was developed, that competition for control of the element began. Sulfur production thus became Sicily's chief industry, and a French company, realizing the value of sulfur to all mankind, gained control of the Sicilian brimstone deposits in 1839 and raised the price of sulfur from \$25 to \$75 per ton. This proved to be a short-sighted policy. Other countries, unable to pay such monopolistic prices for so necessary a product, at once undertook the development of their own sources. They soon learned that sulfuric acid could be made from roasting iron pyrites. As a result, Sicilian sulfur production received a setback from which it has never recovered.

The discovery of these new sources of sulfur did not, however, free America from foreign domination as regards sulfur. More than a quarter-century went by before the first deposit in the United States was even located. Prospectors drilling for oil in Calcasieu Parish, Louisiana, found traces of the mineral in cuttings from their wells in 1867.

Unlike foreign deposits, which are near the earth's surface and easily recoverable by ordinary mining methods, the Calcasieu Parish deposit lies deep underground, under layers of quicksand and deadly hydrogen sulfide gas. Existing mining methods could not be used. Dr. Herman Frasch, a German who came to the U.S., conceived the idea of mining the sulfur not as a solid but as a liquid. To do this, he proposed to melt the mineral underground by means of immense quantities of superheated water injected into the formations. In the face of skepticism and ridicule, Dr. Frasch pushed ahead with his scheme and, in 1894, pumped the first flow of molten sulfur from the Calcasieu Parish deposit. It took eight more years to make the Frasch process an established commercial success.

In about 25 years, the U.S. became a major sulfur producer. But the U.S. has no monopoly, for sulfur is obtained commercially from many sources throughout the world. Native sulfur, or brimstone, produced by the Frasch process in the U.S., is but one of them. The others include pyrites, which are sulfur-containing ores; foreign brimstone; hydrogen sulfide in gases; sulfur dioxide at smelters; sulfate minerals; and elemental sulfur in volcanic deposits.

### Properties

**Allotropy.** Sulfur may appear in a number of different allotropic modifications, that is, in various molecular aggregations which differ in solubility, specific gravity, crystalline form, etc. Like many other substances, sulfur also exhibits dynamic allotropy in that the various allotropes exist together in equilibrium in definite proportions, depending on the temperature in the solid, liquid, and vapor states. Suggested formulas for the various allotropes range from  $S_1$  to  $S_n$ , where  $n$  is a large but unknown

number. The particular allotropes that may be present in a given sample of sulfur depend to a large extent upon its previous thermal history, the amount and type of foreign substances present, and on the length of time that has been allowed for equilibrium to be attained.

In the solid and the liquid states, the principal allotropes are  $S_\pi$ ,  $S_\lambda$ , and  $S_\mu$ . Of these only  $S_\lambda$  is stable (20).  $S_\pi$  rapidly changes into  $S_\mu$  which in turn is converted into  $S_\lambda$ , although at a much slower rate. The allotropes differ in their solubility in carbon disulfide.  $S_\pi$  and  $S_\lambda$  are soluble in carbon disulfide, while  $S_\mu$  is insoluble.  $S_\lambda$  is found in three allotropic crystalline modifications, rhombic ( $S_R$ ), monoclinic ( $S_M$ ), and mother-of-pearl or nacreous sulfur ( $S_N$ ). The latter is actually a type of monoclinic sulfur with axial ratios different from the more familiar  $S_M$  (15). Rhombic sulfur is stable, at atmospheric pressures, up to 95.5°C. (203.9°F.) where the transition to monoclinic ( $S_M$ ) takes place. Monoclinic ( $S_M$ ) sulfur is then stable up to its "natural" melting point of 238.1°F. Nacreous sulfur is metastable at all temperatures up to the melting point.

Three allotropes  $S_\pi$ ,  $S_\lambda$ , and  $S_\mu$  are commonly recognized as existing in dynamic equilibrium in liquid sulfur. (See Table I.) As previously noted, the relative proportions of the various allotropes that may be present depend to a great extent upon the kind and amount of impurities present. Acidic compounds such as sulfur dioxide tend to retard attainment of equilibrium; ammonia tends to hasten it; while iodine brings about a displacement of the equilibrium among the species in favor of increased concentrations of  $S_\mu$ .

TABLE I. Equilibrium Among  $S_\pi$ ,  $S_\lambda$ , and  $S_\mu$  in Molten Sulfur (1).  
(Approximate Concentrations.)

Temp., °F.	Concentration, %		
	$S_\pi$	$S_\lambda$	$S_\mu$
238.1	2.78	97.22	0.0
310	6.2	91.4	2.4
320	6.6	88.9	4.5
360	6.4	71.6	22.0
400	5.9	64.1	30.0
600	4.7	60.0	35.3
800	4.0	59.5	36.5
832	4.0	59.1	36.9

**Constants.** A range of freezing points may be observed, depending upon the composition (percentage composition of  $S_\pi$ ,  $S_\lambda$ , and  $S_\mu$ ) of the liquid sulfur and the crystalline variety ( $S_M$ ,  $S_R$ , or  $S_N$ ) which forms. When the liquid is pure  $S_\lambda$ , the temperatures at which the various modifications are formed are called the "ideal" freezing points. The temperatures at which the crystalline forms are in equilibrium with liquid sulfur containing equilibrium amounts of  $S_\pi$  and  $S_\mu$  are called the "natural" freezing points. Table II gives the "natural" and "ideal" freezing points of the three varieties, as well as other constants.

The viscosity of liquid sulfur (2) is greatly affected by traces of impurities. For specially purified sulfur, the viscosity is about 10 cps at 125°C., drops to a minimum of about 6.7 cps. at about 157°C., and then begins to rise. Between 159 and 160°C.

TABLE II. Physical Constants of Sulfur.

	<i>Ideal</i>	<i>Natural</i>
Freezing point of solid phase, °C.:		
Rhombic, S <sub>R</sub> .....	112.8	110.2
Monoclinic, S <sub>M</sub> .....	119.3	114.5
Nacreous, S <sub>N</sub> .....	106.8	103.4
B.p., °C. (22).....		444.6°C.
Density of solid phase, at 20°C., gram/ml.:		
Rhombic.....		2.07
Monoclinic.....		1.96
Amorphous.....		1.92
Density of liquid, gram/ml., at:		
125°C.....		1.7988
130°C.....		1.7947
140°C.....		1.7865
150°C.....		1.7784
Density of vapor at 444.6°C. and 1 atm., gram/liter.....		3.64
$n_D^{20}$ .....		1.929
Vapor pressure ( $P$ = mm. Hg, $T$ = °K.):		
Rhombic (20–80°C.) (7).....	$\log P = 11.664 - 5166/T$	
Monoclinic (96–116°C.) (17).....	$\log P = 11.364 - 5082/T$	
Liquid (120–325°C.) (22).....	$\log P = 14.7 - 0.0062238T - 5405.1/T'$	
(325–550°C.).....	$\log P = 7.43287 - 3268.2/T$	
Surface tension, dynes/cm., at (5):		
120°C.....		60.83
150°C.....		57.67
Atomic vol., ml.:		
Rhombic.....		15.5
Monoclinic.....		16.4
Crit. temp. °C.....		1040
Crit. pressure, atm.....		116
Crit. vol., ml./gram.....		2.48
Sp.heat, cal./gram-mole/°K.:		
Rhombic (24.9–95.5°C.).....	$C_p = 3.58 + 6.24 \times 10^{-3}T'$	
Monoclinic (–4.5–118.9°C.).....	$C_p = 3.56 + 6.96 \times 10^{-3}T'$	
Liquid (S <sub>L</sub> ) (118.9–44.9°C.).....	$C_p = 5.4 + 5 \times 10^{-3}T'$	
Gas (S) (25–1727°C.).....	$C_p = 5.43 - 0.26 \times 10^{-3}T' - 0.27 \times 10^5 T'^{-2}$	
Gas (S <sub>2</sub> ) (25–1727°C.).....	$C_p = 8.54 + 0.28 \times 10^{-3}T' - 0.79 \times 10^5 T'^{-2}$	
Heat of transformation (rhombic to monoclinic) at 95.5°C., cal./gram.....		2.687
Heat of fusion, cal./gram, at:		
112.8°C. (S (rhombic) → S <sub>L</sub> (liquid)).....		11.9
118.9°C. (S(monoclinic) → S <sub>L</sub> (liquid)).....		9.2
Thermal expansion of rhombic sulfur (linear) at:		
0–13°C.....		$4.567 \times 10^{-5}$
13–50°C.....		$7.433 \times 10^{-5}$
50–78°C.....		$8.633 \times 10^{-5}$
78–97°C.....		$20.67 \times 10^{-5}$
97–110°C.....		$103.2 \times 10^{-5}$
Latent heat of vaporization, cal./gram at (22):		
	<i>L<sup>a</sup></i>	<i>L<sup>b</sup></i>
200°C.....	73.7	—
300°C.....	69.1	—
400°C.....	68.4	66.4
420°C.....	68.7	66.0
440°C.....	69.3	65.6
460°C.....	70.0	65.2



TABLE II. Physical Constants of Sulfur (*Concluded*).

	Natural
Electrical resistivity, ohm (sq.cm.)/cm. at (11):	
20°C.....	$1.9 \times 10^{17}$
110°C.....	$4.8 \times 10^{12}$
440°C.....	$8.3 \times 10^6$
Magnetic susceptibility, c.g.s. units (11):	
Rhombic at 18°C.....	$0.49 \times 10^6$
Monoclinic at 112°C.....	$0.49 \times 10^6$
Liquid at 220°C.....	$0.49 \times 10^6$
Standard electrode potential, S/S <sup>2-</sup> (11).....	0.5 v. (approx.)

<sup>a</sup> Including heat of dissociation to S<sub>2</sub> present in vapor.<sup>b</sup> Minus heat of dissociation to S<sub>2</sub> present in vapor.

the rise is sharp, increasing to 30 cps. at 160°C. and a maximum of about 93,000 cps. at 186–188°C. It then drops off gradually again to about 2000 cps. at 306°C.

**Chemical Properties.** There are four stable isotopes of sulfur, S<sup>32</sup>, S<sup>33</sup>, S<sup>34</sup>, and S<sup>36</sup>, comprising respectively, 95.1%, 0.74%, 4.2%, and 0.016% (18). The relative abundance of the various isotopes has been found to vary slightly depending on the source of the sulfur, the ratio of S<sup>32</sup> to S<sup>34</sup> having a range of 21.61 to 22.60. Three radioactive isotopes of masses 31, 35, and 37 have been generated artificially. The normal orbital electron structure is of the arrangement (2), (2,6), (2,4) (ref. 19). Sulfur has valences of -2, +2, +3, +4, and +6.

Falling between oxygen and selenium in its group, sulfur resembles oxygen in its chemical reactions with most of the elements. Closely related is selenium with its similar group of valences and analogous allotropy. Sulfur is between phosphorus and chlorine horizontally, and its properties are in general what would be expected from its position in the periodic table. An exception is that its melting point is higher than would be expected, probably because of its complex molecular structure (19).

Sulfur is insoluble in water, but it is soluble to varying degrees in many organic solvents, such as carbon disulfide, benzene, warm aniline, warm carbon tetrachloride, and in liquid ammonia. Carbon disulfide is the most commonly used solvent.

Sulfur combines directly and usually energetically with almost all of the elements; exceptions include gold, platinum, iridium, and the inert gases (15). In the presence of oxygen or dry air, sulfur is very slowly oxidized to form sulfur dioxide. When burned in air, it forms predominantly sulfur dioxide with small amounts of sulfur trioxide. In the presence of moist air, sulfurous and sulfuric acids are slowly generated.

Hydrochloric acid reacts with sulfur only in the presence of iron, forming hydrogen sulfide. Sulfur dioxide is formed when sulfur is heated with concentrated sulfuric acid at 200°C. Dilute nitric acid up to 40% concentration has little effect, but sulfur is oxidized by concentrated nitric acid in the presence of bromine with a strongly exothermic reaction (15).

Sulfur combines directly with hydrogen at 150–200°C. to form hydrogen sulfide. At red heat, sulfur and carbon unite to form carbon disulfide, a commercially important reaction. In aqueous solutions of alkali carbonates and alkali and alkaline earth hydroxides, sulfur reacts to form sulfides, polysulfides, thiosulfates, and sulfites.

At normal temperatures, sulfur unites readily with copper, silver, and mercury

and vigorously with sodium, potassium, calcium, strontium, and barium to form sulfides. Iron, chromium, tungsten, nickel, and cobalt react much less readily. In a finely divided state zinc, tin, iron, and aluminum react with sulfur on heating (15).

Various sulfides of the halogens are formed by direct combination of sulfur with fluorine, bromine, and chlorine. No evident reaction occurs with iodine; rather the elements remain as components of a complex mixture. Mixtures of sulfur and potassium chlorate or sulfur and powdered zinc are highly explosive.

The numerous reactions involving sulfur in organic synthesis are commercially significant. Sulfur is important in phases of the processes for the manufacture of lubricants, plastics, pharmaceuticals, dyes, and rubber goods.

Sulfur, itself, is regarded as noncorrosive to the usual materials of construction. Dry, molten sulfur is handled satisfactorily in mild steel or cast-iron equipment. However, acid-generating impurities, which may be introduced in handling and storage, create corrosive conditions. The exposure of sulfur to moisture and air causes the formation of acids which attack a number of metals. To combat such corrosion difficulties, protective coatings of organic compounds, cement, or sprayed resistant metals are often applied to exposed steel surfaces, including pipe and equipment handling liquid sulfur, and to structural members in contact with solid sulfur. Also practical in some applications is the use of resistant metal alloys, particularly of the aluminum and stainless steel groups. Neutralization of the generated acids by the addition of basic chemicals is sometimes employed.

### Analysis

Elemental sulfur in its ore or its refined state can generally be recognized by its characteristic yellow color or by its generation of sulfur dioxide when it is burned in air. Its presence in an elemental state or in a compound can be detected by heating the material with sodium carbonate and rubbing the resulting fused product with water on a silver coin. A black discoloration of the coin indicates the presence of sulfur. This test is quite sensitive.

Quantitatively, sulfur in a free or combined state is generally determined by oxidizing it to a soluble sulfate (by fusion with an alkali carbonate if necessary) and precipitating it as insoluble barium sulfate. Oxidation can be effected with such agents as concentrated or fuming nitric acid, bromine, sodium peroxide, potassium nitrate, or potassium chlorate. Free sulfur is normally determined by solution in carbon disulfide, the latter being distilled from the extract (8).

Generally, crude sulfur contains very small percentages of carbonaceous matter introduced by the sulfur being in contact with traces of oil in its ore body. The amount of this impurity is usually determined by combustion, which requires exacting technique. The carbonaceous matter is oxidized to carbon dioxide and water, the carbon dioxide being subsequently absorbed.

The moisture content of crude sulfur is determined by differential weight of a known sample before and after drying at approximately 110°C. Acid content is determined by volumetric titration with a standard base. Nonvolatile impurities, known as "ash," are determined by burning the sulfur from a known sample, and igniting the residue to remove the residual carbon and other volatiles.

### Occurrence and Extraction

Sulfur found in the native state is normally in well-developed pyramidal or tabular crystals of the orthorhombic system. It is also found in earthy and stalactitic masses. It has a bright yellow color which may be darkened or dulled by impurities; the luster is resinous; and the cleavage is conchoidal or uneven.

Many of the important deposits are associated with limestone, calcite, gypsum, and anhydrite; frequently carbonaceous matter in the form of petroleum or bitumen is a constituent of the sulfur-bearing rock or associated formations. Hydrogen sulfide is also present, usually in solution in the formation waters. In these deposits sulfur is considered to have been derived from the associated sulfate minerals.

Another large group of deposits is comprised of those found in the vicinity of volcanic activity. These have originated from gases and vapors emitted from active craters, solfataras, and hot springs, which have deposited sulfur in the fractures of the rock or in the sediments of lake beds, or by replacement in the rock itself. Common associated minerals are pyrite, marcasite and other sulfides, sulfates, and hydrated siliceous minerals such as opal. Volcanic deposits are usually found in tuffs, lava flows, and similar volcanic rocks, but they may also be found in sedimentary and intrusive formations.

### UNITED STATES

**Salt Dome Sulfur Deposits.** The sulfur deposits associated with the salt domes of the Gulf Coast of Texas and Louisiana are of primary economic importance because of their known and

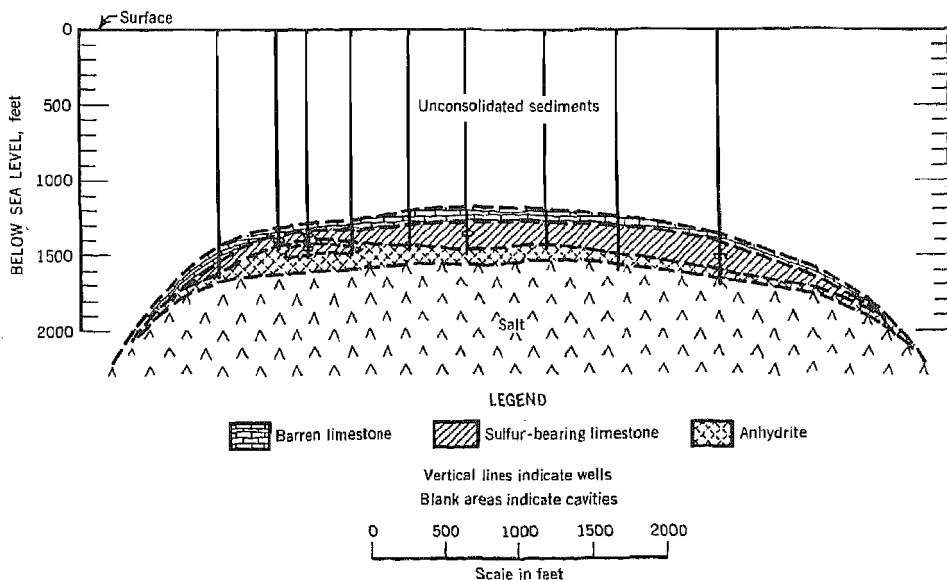


Fig. 1. Cross section of the Grande Ecaille Salt Dome, Plaquemines Parish, La. (14).

potential reserves, their productive capacity, and the unequalled purity of the product as mined. In recent years the output has exceeded 5 million tons annually; from 1894, when sulfur was first produced by the Frasch process, until December 31, 1953, these deposits have yielded 104 million tons.

The domes are composed of coarsely crystalline halite which contains anhydrite as the principal accessory mineral. They are vertical structures, usually circular in outline with steeply dipping

flanks, and they have pierced and intruded the flat-lying unconsolidated sediments of the region, evidently coming from mother salt beds of unknown geologic age lying at great depths. Most of them are surmounted by a caprock formation consisting of anhydrite, which lies in contact with the salt, and gypsum which has been derived from the anhydrite. Limestone in the form of fine-grained gray carbonate interspersed with vugs, seams, fissures, and cavities, which may be partly or wholly filled with calcite, is frequently associated with the gypsum and anhydrite formations. It may be present as a stratum overlying these formations, as lenticular beds covering only a part of them, or as disseminated lenses and nodules included in the upper part of the caprock. It is now generally concluded that the anhydrite caprock was formed as an insoluble residue resulting from solution of the salt by formation waters; that the gypsum has been derived from the anhydrite through hydration; and, although the evidence is not conclusive, the limestone is believed to be derived at least in part from these formations. Figure 1 is a cross section of the Grande Ecaille Dome.

Sulfur of mineralogic interest occurs in the caprocks of most salt domes in the Gulf Coast region, but deposits of sufficient size to warrant commercial development have been found in only a small percentage of them. These deposits usually take the form of tabular lenses, although some differ markedly from this configuration. Sulfur is found in them as well developed crystal aggregates filling the seams and cavities of the porous limestone, and also in the semicrystalline and massive state, filling the openings of the rock. Sometimes commercial mineralization extends into the underlying gypsum, but it has not been found in the dense anhydrite.

These deposits differ markedly in reserves, as illustrated by the domes that have been depleted. Sulfur Dome, Louisiana, with a caprock area of 75 acres, produced 9,412,165 tons; Bryanmound Dome, Texas, with an area of 800 acres, produced 5,001,068 tons; Palangana Dome, Texas, with an area of 1800 acres, produced 236,662 tons; Gulf Dome, Texas, with an area of 300 acres, produced 12,000,000 tons; Jefferson Island Dome, Louisiana, with an area of 400 acres, produced 438,811 tons.

A total of 126 domes are recognized in the Gulf Coast region, nearly all of which have been prospected for sulfur, some more thoroughly than others. In addition to the five depleted ones, referred to in the preceding paragraph, 14 are now being operated as sulfur mines or are being developed for operation. These are:

The Texas Gulf Sulphur Co.:	
Newgulf (Boling Dome)	Wharton County, Texas
Moss Bluff Dome	Chambers County, Texas
Spindletop Dome	Jefferson County, Texas
Freeport Sulphur Co.:	
Bay Ste. Elaine Dome	Terrebonne Parish, La.
Chacahoula Dome	La Fourche Parish, La.
Garden Island Bay Dome	Plaquemines Parish, La.
Grande Ecaille Dome	Plaquemines Parish, La.
Hoskins Mound Dome	Brazoria County, Texas
Nash Dome	Fort Bend County, Texas
Jefferson Lake Sulphur Co.:	
Clemens Dome	Brazoria County, Texas
Long Point Dome	Fort Bend County, Texas
Starks Dome	Calcasieu Parish, La.
Duval Sulphur & Potash Co.:	
Orchard Dome	Fort Bend County, Texas
Standard Sulphur Co.:	
Damon Mound	Brazoria County, Texas

During the past few years the structures found in the saline basin of the Isthmus of Tehuantepec, Veracruz, Mexico, have been prospected for sulfur, and on several of them discoveries have been announced. These include the San Cristobal-Capoacan Dome by the Mexican Gulf Sulphur Co., the Jaltipan Dome by Pan American Sulphur Co., and the Salinas or Amozquite Dome by Gulf Sulphur Corp. Mexican Gulf Sulphur Co. started production on a modest scale early in 1953, and Pan American Sulphur Co. started mining operations later in 1953. Mexico is potentially a major source of elemental sulfur. Salt domes and similar structures are known in regions other than the Gulf Coast and Tehuantepec, but sulfur deposits that are worthy of being developed have not been discovered in any of them.

**The Frasch Process.** Normal practices in applying the Frasch process to mining these deposits have been abundantly described in the literature. The primary

requisite is a power plant to supply the large volume of hot water required, together with compressed air for pumping molten sulfur from the wells, and electric power for drilling, lighting, operating maintenance equipment, loading sulfur for shipment, and similar operations.

A typical setting of equipment in a sulfur well and the principles of mining are illustrated schematically in Figure 2. Water, at a temperature of around 325°F. and under pressure of 250 p.s.i., which is injected through the 8-in. water line, flows out into the porous sulfur formations through the perforations in the bottom. Once the temperature of the formations in the vicinity is raised above the melting point of sulfur, liquid sulfur, being approximately twice as heavy as water, sinks through the porous rock, and collects in a "pool" at the bottom of the well. As soon as the level of the pool rises to submerge the bottom of the sulfur line, formation pressure forces the molten sulfur to ascend part way up the line. From this point it is pumped to the surface by compressed air introduced through the air line. The hot water injected for mining is withdrawn from the deposit through bleed wells, which customarily are drilled at localities remote from the mining area where temperature is lower, so that the greatest amount of heat possible can be retained in the deposit. On the surface, liquid sulfur is transported through steam-heated lines to a separator where the air is removed, and then it is pumped to storage bins (frequently called vats) where it is permitted to solidify. Sulfur produced at mines situated in the marshes, where conditions of terrain are adverse, is transported in the liquid state in barges to storage bins conveniently located for shipment.

The capacities of power plants now being operated at sulfur mines vary between 1.75 million and 10 million gallons of hot water daily. Gulf Coast deposits are generally fortunate in being situated close to rivers from which the large requirements of fairly pure water can readily be obtained. Before being heated, the water is treated to control corrosion and scale; modern power plants employ high-pressure boilers to raise the temperature to above 300°F. About one-fourth of the volume of water is converted to steam in these boilers, and then in mixing-type heaters the steam raises the temperature of all the water to that required for mining. Steam is also furnished to centrifugal pumps which deliver the hot water through thousands of feet of insulated pipe to the wells. Steam-

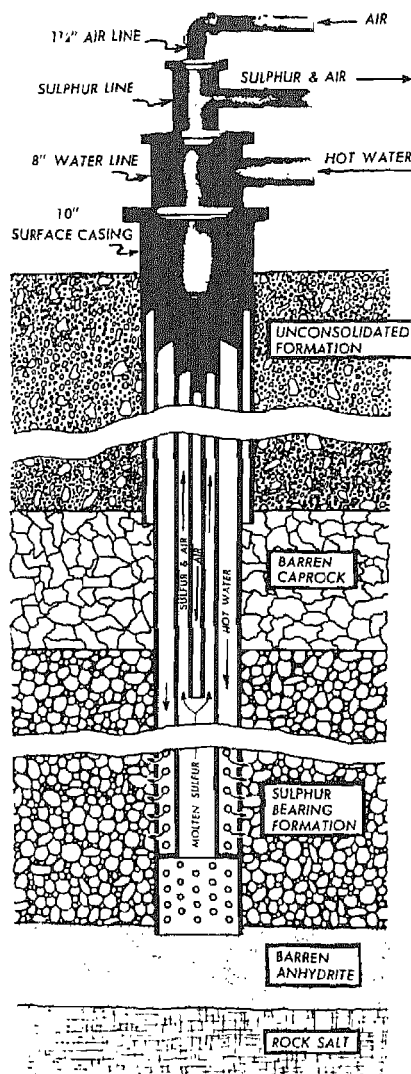


Fig. 2. Typical method of equipping sulfur well (14).

driven compressors supply compressed air; steam is also used to generate electric power. The heat in the steam exhausted from these machines, as well as that carried in the flue gases, is reclaimed to preheat the water, a practice that gives modern sulfur mining plants a high degree of efficiency.

At the Bay Ste. Elaine Dome, the small size of the deposit and its remoteness from a supply of fresh water introduced problems that led to construction of a portable-type plant installed on a large steel barge. In this plant, sea water is heated to 325°F. for the purpose of mining sulfur. To overcome excessive corrosion, oxygen is removed from the raw sea water by bringing it in contact with combustion gases in a packed tower. Then, preheated by these gases, its temperature is raised to 325°F. in indirect heat exchangers, using steam furnished by high-pressure boilers. Condensate from the heat exchangers is recycled to the boilers, and fresh water requirements are limited to those lost in leaks and to other small losses in the system. The process being used here frees sulfur mining from dependence on a large volume of water of a quality that can be made suitable for high-pressure boilers.

Sulfur produced from Gulf Coast deposits is free from arsenic, selenium, and tellurium and has an exceedingly small ash content. Carbonaceous matter derived from associated hydrocarbons is the principal impurity.

#### SULFUR DEPOSITS OF SICILY

The sulfur deposits of Sicily have been worked since ancient times. In the 19th century they constituted the world's most important source of brimstone. Peak production of 537,000 tons was achieved in 1899, but a few years thereafter, when much cheaper sulfur from salt domes of the Gulf Coast region supplanted the Sicilian in world markets, the output began its steady decline. In its long history the district is credited with having produced more than 40 million tons of brimstone; nevertheless, geologists still consider it to have a large potential reserve of ore. Caltanissetta is the principal seat of mining activity, and other important centers are Lercara, Agrigento, and Racalmuto. The sulfur, associated with calcite, gypsum, bitumen, and celestite, is found in sedimentary beds of Upper Miocene age. Mining is by the cut-and-fill method, and the sulfur is recovered from the ore by vaporization, utilizing part of the sulfur as fuel.

#### JAPANESE SULFUR DEPOSITS

Deposits of volcanic origin are found in many parts of the world. Some of them are worked profitably and are of importance to the countries in which they are found; however, most are situated in isolated regions and at high elevations where costs of production and transportation are prohibitive. Among this group, however, the deposits of Japan take first place by virtue of their long productive history and the important tonnages that have been won from them in modern times. Japanese sulfur deposits are found in a part of the volcanic region that borders the Pacific Ocean on the west and north. Most of the deposits are opened by tunnels, and mining is carried on by the room-and-pillar, chamber-and-pillar with filling, and cut-and-fill systems. Very little mechanization is applied to the work. Sulfur is extracted from the ore by a distillation process. It is carried on in rows of cast-iron pots 3 ft. in diameter by 2 ft. deep, each of which holds about 400 lb. of ore. Each row of pots is connected to a condensation chamber, a steel cylinder 2 ft. in diameter lying beside the row outside the furnace. A short length of pipe connects each pot with its condenser. Brickwork

is used to form flues which conduct combustion gases back and forth under the pots. Sulfur vapor flows from the pot to the condensation chamber in which the condensed liquid sulfur is collected. The average grade of ore treated lies between 25 and 35% S.

#### OTHER SULFUR DEPOSITS

Sulfur is also produced from surface deposits in the U.S.S.R., France, Mexico, western U.S., and the Andes Mountains of Colombia, Ecuador, Chile, Peru, Bolivia and Argentina. Processes used include flotation, distillation, autoclaving, filtration and solvent extraction.

One of the more recent flotation processes was developed by the Chemical Construction Company. The ore is ground to -28 mesh, suspended in water to form a slurry, and then pumped to a coil-type gangue separator. Live steam is injected into the pulp, the sulfur melting and agglomerating into globules separate from the gangue. The pulp is then quenched and screened. The oversize is melted and filtered along with a flotation concentrate produced from the fines. Flotation of the fines is carried out in standard equipment, using pine oil, fuel oil, or Aerofloat reagents.

#### RECOVERY OF SULFUR FROM SOUR GASES AND FROM SULFIDE ORES

In addition to deposits of the native element, other sources, such as sour natural gas, refinery gas, pyrites and other sulfide ores, and smelter-stack gases, are

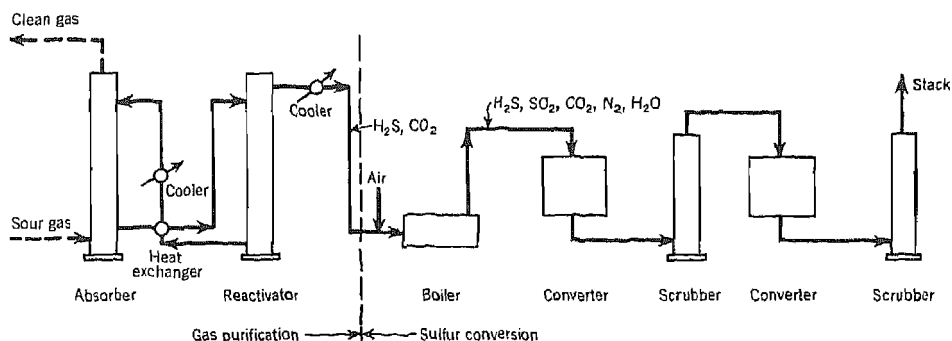


Fig. 3. Preparation of sulfur from hydrogen sulfide (generalized flow sheet).

today furnishing brimstone for world markets. In the U.S. sour natural gas and refinery gas, in which the sulfur is present as hydrogen sulfide, constitute an important source.

**Sour and Refinery Gases.** Conversion of hydrogen sulfide into sulfur was developed in England and Germany more than 100 years ago, and through the years improvements in the original process have resulted in smaller and more efficient plants (see Fig. 3). In the first step of the process, hydrogen sulfide is removed from the raw gas. There are a number of methods for accomplishing this, one being to absorb the hydrogen sulfide in a solution of an alkylamine. On being heated the pregnant amine solution gives up its hydrogen sulfide in concentrated form, as well as any carbon dioxide that may have been present in the raw gas. The concentrated hydrogen sulfide is then fired in a combustion chamber, and burned in such a manner that one-third of the volume is converted to sulfur dioxide. After cooling, the products of combustion are passed through a converter, packed with a catalyst, in which the hydrogen

sulfide and sulfur dioxide react to produce sulfur vapor and water vapor. Sulfur vapor is condensed by washing with liquid sulfur. From practically nothing in 1940, the production of sulfur by this general process had increased to 337,099 tons per year in 1953 (3a, 17a). See also *Gas cleaning and purification*.

There are other processes, of very little importance in the U.S., for recovering hydrogen sulfide or sulfur from coke or producer gases, including the Thylox, sodium phenolate, and related systems. The Thylox process utilizes an arsenical solution to absorb the hydrogen sulfide from the gases. The pregnant solution is oxidized to release elemental sulfur as a froth, which is removed before recycling the absorbent. The sulfur is used as a paste (for insecticides) or fused and converted to a dry solid form. This type of process is of importance in Europe.

*The Orkla Process.* A process for producing sulfur from cuprous pyrite was developed by the Orkla Mining Co. at Thamshavn, Norway, and the output, ranging from 80,000 to 100,000 tons annually, has furnished an important part of European requirements. The process has also been put in operation by Rio Tinto Co., Ltd., at its mines near Huelva, Spain, and by Mason & Barry, Ltd., in Portugal, however on a smaller scale than Orkla's.

The process involves recovery of approximately 80% of the sulfur content of a pyritic copper ore by direct smelting in the presence of a carbonaceous reducing agent. A charge consisting of ore, flux, and coke is introduced into a shaft furnace. In the upper half of the shaft it is heated to 900–1400°F., this temperature being sufficient to drive off the sulfur that is feebly bound in the pyrite. The sulfur dioxide formed in the bottom zone is reduced by coke in the center section of the furnace where the temperature ranges from 1300 to 2000°F. True smelting takes place in the bottom, or bosh section, where the heat from the oxidation of iron and sulfur is sufficient to form copper matte and slag, which are handled conventionally.

The waste gas contains a complex series of carbon, oxygen and sulfur compounds, among which carbon monoxide, carbon oxysulfide, carbon disulfide, hydrogen sulfide, and sulfur dioxide are most abundant. The gas is passed through a catalytic chamber, where at a temperature of 850°F. the sulfur dioxide reacts with the other compounds, oxidizing the carbon and hydrogen and forming elemental sulfur in the vapor state. The sulfur is condensed in waste-heat boilers and Cottrell precipitators.

*The Noranda Process.* It has long been known that pyrite when heated in the absence of oxygen to about 1000°F. will evolve about half of its sulfur in elemental form. Noranda Mines, Ltd., and Battelle Memorial Institute developed a process based upon this property to recover elemental sulfur from pyrite. The first commercial plant was built at Welland, Ontario, in 1954. The reactions involved are approximated by  $8\text{FeS}_2 \rightarrow \text{S}_8 + 8\text{FeS}$  and  $3\text{FeS} + 5\text{O}_2 \rightarrow \text{Fe}_3\text{O}_4 + 3\text{SO}_2$ . The heat of reaction of the second equation furnishes the heat necessary for the first. The  $\text{SO}_2$  containing gases are used for the production of sulfuric acid.

Fine pyrite concentrates are pelletized with water and charged to the pallets of a Dwight-Lloyd sinter machine. After ignition of the charge, the pallets pass through the wind boxes of the machine, where a mixture of air and recycle gas passes down through the pallets. The recycle gas reduces temperature, thus preventing fusion of the iron oxide, and also helps to prevent oxidation of the sulfur vapor. The combustion, or oxidation zone, proceeds downward through the charge in a distinct wave, distilling elemental sulfur ahead of it. The gases from a pallet just entering the wind box may be at a temperature of about 600°F., whereas those from a pallet just before



leaving may be about 1800°F.; the average temperature of the gases when leaving the machine is thus about 1000°F. The gases, containing SO<sub>2</sub>, N<sub>2</sub>, and sulfur vapor, are cooled in a waste heat boiler to condense the sulfur vapors, after which part is recycled and part sent to the sulfuric acid plant. The cinder leaving the machine contains residual sulfur and may be sintered on a separate machine to produce merchantable iron ore. About 40% of the total sulfur in the pyrites may be recovered as elemental sulfur and about 50% as sulfuric acid. See Vol. 8, pp. 225-27.

### Economic Aspects

World sulfur production has undergone a series of drastic changes since about 1900. At that time world production of sulfur in all its forms probably ranged between 2 and 2½ million tons annually. In 1952, world sulfur production amounted to nearly 12½ million tons. In 1900, the world was dependent largely upon the sulfur deposits of Italy and Sicily and the pyrites deposits of the Iberian peninsula. The development of a practical method for mining the sulfur deposits of the Gulf Coast area of the U.S. brought about a rapid change in the world's source of sulfur. In the years subsequent to World War II, U.S. brimstone supplied over one-fourth of the world sulfur, although the nations other than the U.S.S.R. and its satellites obtained most of their sulfur from other materials, primarily pyrites. During World War II, the production of sulfur-containing materials outside of America was badly disrupted and recovery of production after cessation of hostilities was slow. Furthermore, acid plants using brimstone are less costly to build and to operate than plants using pyrites or other sulfur materials. American brimstone is also the cheapest and purest of all the various forms of sulfur. Accordingly, the foreign consumers in rehabilitating and expanding their sulfuric acid industry turned more and more to the use of American brimstone. By mid-1950 when the Korean crisis developed, exports of American brimstone had almost doubled as compared with the tonnage exported immediately preceding the outbreak of World War II.

During this time when the foreign consumers were becoming more dependent on American sulfur, the sulfur requirements of American industry were likewise expanding. In the decade 1940-1950 sulfur consumption doubled in the U.S. The growth in sulfur use was much greater than the growth in the use of minerals in general. The American brimstone industry had increased its output by 1950 to about two-and-one-half times the average for the prewar years 1935-1939, but this increase in production was not sufficient to meet the expanded demand for its product. Accordingly, in order to meet the market demand, sales were made from stocks of sulfur above ground which drastically reduced the stocks to about a six months' supply.

After the outbreak of the Korean war in 1950, it became evident that the full world demand for American brimstone could not be met. During 1951, the United States Government instituted a sulfur allocation system, under which sulfur producers were directed to ship specified tonnages. At the beginning of 1952, the government further restricted the use of sulfur, limiting domestic consumption to a basis of 90% of the amount used in 1950, and adopted the policy of maintaining existing stocks of mined sulfur.

In the meantime the outlook for sulfur supplies improved greatly. The shortage stimulated exploration and development of new brimstone mines. Other projects to obtain sulfur in some form from refinery gases, smelter gases, sour natural gases, sur-

face deposits, pyrites, and sulfate minerals were developed in the U.S. as well as in other free-world countries. Simultaneously, measures for the conservation of sulfur progressed which led to the recovery and re-use of spent sulfuric acid and to improved efficiency in the use of sulfur in the various consuming industries.

The improvement in the world sulfur situation led to the decontrol of sulfur in the U.S. market in November 1952. International allocation of sulfur was discontinued early in 1953, although the U.S. maintained limited controls on exports of American brimstone for a further period.

The demand for sulfur is expected to grow. Studies indicate a normal growth of sulfur consumption in the U.S. equivalent to about 3% per year or approximately the same as the long-term trend in over-all industrial output. In the decade 1940-1950, sulfur consumption deviated considerably from industrial output as measured by the Federal Reserve Index. Sulfur consumption dropped considerably below the Federal Index during World War II, when the latter index was abnormally inflated by the output of war materials. After World War II sulfur consumption moved ahead of the Federal Reserve Index. For the decade as a whole, the rate of growth in sulfur consumption was about twice the long term growth.

The President's Material Policy Commission in its report "Resources for Freedom" concluded that sulfur demand is expected to grow so vigorously that "twice as much sulfur will probably be required in 1975 as in 1950 both in the United States and in the rest of the world."

There need be no shortage of supplies. The low-cost American brimstone may not continue to supply as large a portion of the world's sulfur as in the past, for only limited salt dome areas remained unprospected, and existing mines face ultimate depletion. Consequently, the trend toward higher-cost forms of sulfur is likely to continue.

Over three-fourths of the sulfur consumed by industry is first converted to sulfur dioxide, primarily for sulfuric acid and sulfite pulp. For these uses, sulfide ores, sulfate minerals, and impure sulfurs can be used. Elemental sulfur is used for economic reasons only. For carbon disulfide, insecticides, and many chemicals, elemental sulfur must be used. Therefore, if and when elemental sulfur production wanes, more of the burden for acid uses will be taken up by alternate sulfur-bearing materials, with the elemental sulfur going to uses for which it is essential. U.S. production, consumption, and prices are shown in Tables III, IV, and V. Data for Tables III and IV are from

TABLE III. U.S. Production and Disposition of Crude Sulfur.  
(Long Tons.)

Year	Production of crude sulfur	Shipments of crude sulfur		Total	Stocks at mines
		Domestic	Foreign		
1901	6,866	6,866	—	6,866	<sup>a</sup>
1910	247,060	220,177	30,742	250,919	<sup>a</sup>
1920	1,255,249	1,040,175	477,450	1,517,625	<sup>a</sup>
1930	2,558,981	1,396,605	593,312	1,989,917	1,928,000
1940	2,732,088	1,812,274	746,468	2,558,742	4,200,000
1950	5,193,256	4,063,718	1,440,996	5,504,714	2,654,530
1951	5,279,614	3,705,028	1,283,073	4,988,101	2,837,432
1952	5,293,145 <sup>b</sup>	3,837,238	1,304,154	5,141,392	3,068,855
1953	5,155,342 <sup>b</sup>	3,982,698	1,241,536	5,224,234	3,022,486

<sup>a</sup> Not available.

<sup>b</sup> Does not include sulfur content of low-grade ores produced in western mines.

TABLE IV. U.S. Estimated Consumption of Sulfur in All Forms.  
(Long Tons.)

Year	Sulfur in pyrites		Native sulfur		Other elemental	Sulfur in gases	Total
	Domestic	Foreign	Domestic	Foreign			
1901	93,000	181,700	6,866	167,712	—	9,300	459,478
1910	96,600	328,300	220,177	28,800	—	84,100	757,977
1920	124,300	149,700	1,040,175	77	—	216,200	1,530,452
1930	125,000	165,700	1,396,605	1,163	2,500	205,800	1,896,768
1940	263,100	183,200	1,812,274	35	3,528	206,718	2,468,855
1950	374,800	100,200	4,198,963	25	78,560	255,889	5,008,437
1951	432,800	106,300	3,812,274	2,106	194,000	300,413	4,847,893
1952	418,000	140,622	3,757,568	4,863	225,626	313,200	4,859,879
1953	434,000	92,000	3,883,000	1,229	325,000	335,000	5,070,229

TABLE V. Annual Average Prices of Domestic Crude Brimstone.

Year.....	1913	1930	1940	1950	1951	1952
Price per long ton, \$ <sup>a</sup> .....	22.00	18.00	16.00	18.90	21.00	21.00

<sup>a</sup> Official Bureau of Labor Statistics data. Price is f.o.b. mine.

*Minerals Yearbook*, U.S. Bureau of Mines and *Mineral Resources of the United States*, U.S. Geological Survey.

### Specifications and Standards

Specifications for commercial grades of sulfur are given below.

*Crude, run-of-mine*—"Bright" 99.5% pure. "Dark" contains up to 1% C. Both bright and dark sulfur free of arsenic, selenium, and tellurium.

*Refined sulfur*—Elemental sulfurs produced by distilling crude sulfur. Purity not less than 99.8%. Generally free-burning. Available in lumps and cast sticks. Used where sulfur is burned in small quantities for fumigation, bleaching, etc.

*Sublimed sulfur, flowers of sulfur*—Refined sulfur in fluffy powdered form; contains up to 30% of the allotropic form insoluble in carbon disulfide. Used in medicinal preparations, stock feeds, cutting oils, and dusting sulfurs.

*Flour sulfur*—Ground refined or crude sulfurs. Grades and fineness depend upon brand. Available in grades of 90% minus 80 mesh, 100% minus 100 mesh, 85% minus 200 mesh, etc.

*Rubbermakers sulfur*—Ground sulfurs of various finenesses with special specifications of low acid, ash, moisture contents.

*Insoluble sulfur*—Sulfurs containing up to 85% carbon disulfide insoluble-matter. For special purposes in the rubber trade.

### Health and Safety Factors

Sulfur in itself is virtually nontoxic and can be taken internally without injury. It is only slightly diuretic. No mention has been found in the literature of systemic poisoning due to inhalation of sulfur powder. It is, however, capable of irritating the ocular conjunctivae and the mucous membranes of the respiratory passages. Powdered sulfur may occasionally produce an irritant action on the skin which in certain cases may take an eczematous form in predisposed individuals. However, elementary sulfur when taken internally or even when in external contact with the body may

form hydrogen sulfide and other sulfur compounds. The quantity of hydrogen sulfide formed is probably a function of the exposed surface area of the sulfur. It seems possible, therefore, that appreciable quantities of very fine sulfur taken internally could be toxic. When sulfur burns, it forms sulfur dioxide which is instantaneously dangerous at concentrations of 400 p.p.m. and above. For periods of one-half to one hour, 50-100 p.p.m. is the maximum allowable concentration. Because of the low ignition temperature of sulfur and its tendency to develop static charges, sulfur dust presents a fire and explosion hazard. Inert atmospheres are useful and sufficient when grinding or processing sulfur powders. See reference (16).

### Uses

The largest single use of sulfur is for the production of sulfuric acid. All the various sulfur-bearing materials may be used for this purpose and the choice of one material as contrasted with another is determined by economic factors such as price, availability, and dependability.

About 75% of the sulfur consumed in the U.S. is converted into acid. The capacity of the U.S. for the production of virgin sulfuric acid amounted to 13,400,000 short tons (100%  $\text{H}_2\text{SO}_4$ ) in the beginning of 1951. The Defense Production Administration has requested an increase in capacity of 4,100,000 tons by January 1, 1955, which would bring total capacity to 17,500,000 tons. These tonnage figures do not include the quantities of spent sulfuric acid that are recovered for further economic use. This spent (or reclaimed) acid may be used as such, combined with new acid before use (fortified acid), or in some instances decomposed to produce new acid. It is estimated that the quantity of spent acid recovered in 1952 was in the order of 2,400,000 tons.

The principal industries using elemental sulfur as such include wood pulp, carbon disulfide, insecticide and fungicide, rubber, metallurgical, fireworks, and petroleum refining.

Ground crude sulfur, precipitated pastes, and flowers of sulfur are important constituents of fungicides and insecticides. The ground sulfurs are usually compounded with various wetting and sticking agents. Raymond mills, utilizing a low-oxygen gas to prevent fires, are often used for grinding, as are jet impact mills such as the Micronizer. Flowers of sulfur are produced by passing sulfur vapors into large chambers, where they condense in the form of a fine "snow" and from where they are periodically removed, screened, and boxed for shipment.

The rubber industry also requires large quantities of ground sulfur for compounding and vulcanizing. This industry also uses sulfur in the form of various organic compounds. See *Rubber chemicals*.

The petroleum industry, besides being a large consumer of sulfuric acid, also uses elemental sulfur and sulfur dioxide; for example, in the "doctor" treatment of gasoline (see Vol. 10, p. 144) and, as sulfur dioxide in the Edeleanu process for removing aromatics from kerosene. Compounded with phosphorus, sulfur is used in the manufacture of certain heavy duty lubricants.

Sulfur is used in the flotation of ores to control pH; in the production of magnesium from sea water; in the smelting of lead and other ores; in the production of free-machining steels; in the treatment of boiler and cooling waters; to stabilize styrene monomer; for the impregnation of paper board and wall board; and even in the preparation of permanent-wave compounds.

## Bibliography

- (1) Aten, A. H. W., *Z. physik. Chem.*, **86**, 1-35 (1914).
- (2) Bacon, R. F., and Fanelli, R., *J. Am. Chem. Soc.*, **65**, 639-48 (1943).
- (2a) Bartlett, L., and Feierabend, R. H., "Development and Operation of Sulphur Deposits in the Louisiana Marshes," *Mining Eng.*, **4**, 775-83 (1952).
- (3) Bridgman, P. W., *Proc. Am. Acad. Art Sci.*, **62**, 207-26 (1927); **72**, 207-25 (1937); *Phys. Rev.*, **57**, 237-39 (1940).
- (3a) *Chem. Eng.*, **59**, 210-13 (1952).
- (4) Dunning, J. R., and Paxton, H. C., *Matter, Energy and Radiation*, McGraw-Hill, N.Y., 1941, pp. 623.
- (5) Fanelli, R., *J. Am. Chem. Soc.*, **72**, 4016-18 (1950).
- (6) Forbath, T. P., *Trans. Am. Inst. Mining Met. Engrs., Mining Eng.*, **5**, 881-85 (1953).
- (7) Fourietier, G., *Compt. rend.*, **218**, 194-96 (1944).
- (8) Friend, 1931, Vol. VII, Part II, pp.
- (9) Gmelin, 8th ed., 1952-53, System-Nummer.
- (10) Haynes, W., *The Stone that Burns*, Van Nostrand, N.Y., 1942.
- (11) *International Critical Tables*.
- (12) Kelley, K. K., "Contributions to the Data on Theoretical Metallurgy—X. High Temperature Heat Content, Heat Capacity, and Entropy Data for Inorganic Compounds," *U.S. Bur. Mines Bull.*, **476** (1949).
- (13) Kondratjew, V., *Z. physik. Chem.*, **B7**, 70-73 (1930).
- (14) Landy, W. T., "Sulphur and Pyrites," in *Industrial Minerals and Rocks*, 2nd ed., A.I.M.E., 1949, ch. 47. (Contains an extensive bibliography of the geology and mining of sulfur.) Figs. 1 and 2 courtesy American Institute of Mining & Metallurgical Engineers.
- (15) Mellor, 1930, Vol. X, pp. 27, 87-95, 651.
- (16) National Safety Council, "Handling and Storage of Sulfur," *Industrial Data Sheet*, **D-P.P.-5** (1945).
- (17) Neumann, K., *Z. physik. Chem.*, **A171**, 416-20 (1934).
- (17a) Sawyer, F. G., Hader, R. N., Herndon, L. K., and Morningstar, E., *Ind. Eng. Chem.*, **42**, 1938-50, 1950.
- (18) Seaborg, G. T., *Revs. Mod. Phys.*, **16**, 1-32 (1944).
- (19) Thornc, P. C. L., and Ward, A. M., *Inorganic Chemistry*, 3rd ed., Nordeman, N.Y., 1939, p. 6.
- (20) Tuller, W. N., *The Sulphur Data Book*, McGraw-Hill, N.Y., 1954.
- (21) West, J. R., *Ind. Eng. Chem.*, **42**, 713-18 (1950).
- (22) West, W. A., and Menzies, A. W. C., *J. Phys. Chem.*, **33**, 1880-92 (1929).

F. L. JACKSON, E. H. THAETE, JR., L. B. GITTINGER, JR.,  
L. A. NELSON, JR., AND H. BLANCHET

SULFURATION. See *Sulfur dyes*.

## SULFUR COMPOUNDS—STRUCTURE

This article deals with the structural and theoretical chemistry of sulfur compounds in general (4a,8,12,15,19,21,22). See also *Sulfur compounds, inorganic*; *Sulfur compounds, organic*.

Many of the properties of sulfur in its compounds are readily understandable from its position in the periodic classification of the elements. This is best seen by enumerating the ways in which the second period sulfur atom differs from the first period oxygen atom. Both oxygen and sulfur, the first two members of the sixth group of elements, bear a strong, but actually superficial, resemblance in that each possesses a similarly constituted outer shell of six valence electrons. The essential differences are: (1) the increased size and weight of sulfur over oxygen, (2) the greater screening of the nuclear charge by the eight extra electrons of sulfur in its completed shells of nonvalency electrons, and (3) the availability to sulfur, but not to oxygen, of relatively accessible unoccupied *d* orbitals. See also *Valence*.

The electronic structure of sulfur may be represented by:

Shells:	<i>K</i>			<i>L</i>		<i>M</i>			
Orbitals:	1s <sup>2</sup>	2s <sup>2</sup>	2p <sup>6</sup>	3s <sup>2</sup>	3p <sub>x</sub> <sup>2</sup>	3p <sub>y</sub>	3p <sub>z</sub>		
	"Neon" core			Valence electrons					

According to the exclusion principle, the *s* orbital can provide only one bond and the *p* orbitals a maximum of three. Six-bonded sulfur as in SF<sub>6</sub> arises from the promotion of 3*s* and 3*p* electrons into vacant 3*d* orbitals. There are good grounds for believing that very many sulfur compounds utilize *d* orbitals with expansion of the normal octet of valence electrons up to 10 and in some cases to a maximum of twelve shared electrons (6,10,14).

A similar situation exists between first-period nitrogen and second-period phosphorus, both with 5 electrons in their outer or valence shells. Nitrogen, like other elements of the first short period, having only *s* and *p* orbitals available for bond formation, can form no more than 4 covalent bonds with a maximum of eight shared electrons in compound formation. Phosphorus in the second short period, however, expands its valence shell to ten electrons in its pentahalides and in the PF<sub>6</sub><sup>-</sup> ion. Resonance forms involving a similar expansion undoubtedly play an important part in many compounds of phosphorus involving P—O bonds (see *Phosphorus compounds, inorganic*, Vol. 10, p. 461).

The widespread recognition that elements of the second short period can and do violate the octet rule (which applies strictly to elements of the first short period) in many of their compounds with the more electronegative elements, such as fluorine, oxygen, chlorine, and nitrogen, and even sulfur in some cases, has been a most important development of recent years. In the case of sulfur, this has helped to make explicable much of the chemistry of its compounds (see below). This development is so recent, that is since the late 1940's, that many modern textbooks still formulate all sulfur compounds, with the exception of SF<sub>6</sub> and S<sub>2</sub>F<sub>10</sub>, exclusively within the confines of the octet rule, employing the semipolar or dative bond as a single covalent bond. This was largely based on comparison between the planar structure of three-bonded species, such as COCl<sub>2</sub>, CO<sub>3</sub><sup>2-</sup>, and NO<sub>3</sub><sup>-</sup>, and the pyramidal structure of all three-bonded sulfur compounds (with the exception of SO<sub>3</sub>), including such types as R<sub>3</sub>SO, SOCl<sub>2</sub>, SO<sub>3</sub><sup>2-</sup>, and R<sub>3</sub>S<sup>+</sup> (21). The definite establishment of ten valence electrons in some of these three-bonded sulfur compound structures has, however, vitiated these arguments based on such superficial comparisons, even though the reasons for the nonplanar structure of these sulfur compounds are not yet fully understood (19).

Some of the more important consequences of the above-described features of the sulfur atom are:

(1) Sulfur exhibits a fairly pronounced tendency to form chain compounds containing covalent S—S linkages. These are exemplified in the polysulfides, the polythionates, and the various forms of elemental sulfur. This can be ascribed to the ready

formation of low-energy, obtuse-angled  $sp$  orbital bonds, in place of right-angled  $p$  orbital bonds. By utilizing available low-energy  $d$  orbitals (13) these linkages acquire a partial double-bond character, that is, the sulfur valence shell is increased to 10 electrons and the bond acquires a degree of resonance energy which contributes to its stability. This chain-forming tendency is virtually absent in oxygen and is very marked in selenium and tellurium which form stable infinite-chain molecules.

(2) Most oxygen compounds exhibit a covalency of two. Oxonium (onium) compounds,  $[R_3O]^+$ , show a covalency of three, but 4-covalent oxygen is very uncommon. Sulfur, on the other hand, exhibits covalencies of 2, 3, 4, and 6. This makes for a large number of compounds in which the sulfur atom is central rather than terminal.

(3) Sulfur lacks any tendency to form hydrogen bonds. This is exemplified by the nonassociated character of hydrogen sulfide and the mercaptans, and may account in part for the greater acidity of hydrogen sulfide over water and of mercaptans,  $RSH$ , over alcohols,  $ROH$ . Oxygen compounds of sulfur display some hydrogen bonding ability, and hydrogen bonds undoubtedly are present in the more stable oxyacids of sulfur, such as the low-melting crystalline peroxy-sulfuric acids. The inability of sulfur to form hydrogen bonds may also account in part for the nonexistence of hydrosulfides of the heavy metals; only ionic hydrosulfides are known, and these form only with the most electropositive of the metals.

(4) Sulfur compounds are considerably more covalent than are the analogous compounds of oxygen. Sulfur forms ionic bonds only with the most electropositive elements, namely the alkali and alkaline earth metals. At the other extreme, the bonds formed with fluorine, the most electronegative of the elements, are substantially covalent as evidenced by the pyramidal structure of  $SOF_2$  analogous to that of  $PF_3$  and  $AsF_3$  (ref. 22, p. 297).

(5) Sulfur has a low-to-moderate degree of electronegativity. The nature of compounds formed between sulfur and the other elements can be understood in a general way by reference to the electronegativity values. Values derived by Pauling (12) for sulfur and the principal elements forming compounds with it are: F 4.0, O 3.5, Cl 3.0, N 3.0, S 2.5, C 2.5, P 2.1, and H 2.1. The metals have electronegativity values below 2.0.

The moderate electronegativity of sulfur, taken with the availability to it of low-energy  $d$  orbitals, thus accounts in a general way for the observed polymerizing tendency of sulfur, for its combination of reactivity and stability, and for the general properties of its molecular compounds, namely, their nonassociated, nonpolar, nonhydrogen-bonding character. Other consequences of this combination of features are the strong tendency of sulfur to form covalent bonds with most of the elements and even semimetallic bonds with some of the transition metals. The most striking consequence of all is the unique thermal and allotropic behavior of sulfur itself. Elemental sulfur is recognized today as a reversibly labile group of polymeric molecular groups of sulfur atoms, namely puckered or staggered  $S_8$  rings and  $S_n$  chains, whose equilibrium composition is a function of temperature and pressure (1,13) (see also *Sulfur*).

### Classification

Practically all sulfur compounds, both inorganic and organic, can be divided, largely on the basis of structure, into two main classes, namely molecular or finite compounds and nonmolecular or infinite crystal-lattice compounds. All of the molec-

ular compounds, of which sulfur dioxide is an example, are nonionic covalent-bonded compounds. Most of the important properties of this group are due to these bonds and are properties of the finite discrete molecules.

Forming a transition between the finite molecular and the infinite nonmolecular classes of sulfur compounds are the high-polymeric molecular compounds of sulfur, of which solid sulfur trioxide is an example.

The nonmolecular compounds of sulfur are conveniently divided into those that are water-soluble and those that are insoluble. There is a sound reason for this seemingly nonstructural classification. The water-soluble group, of which sodium sulfite is a typical example, are of interest mainly in solution, wherein the ions function as finite charged molecules. The bonds in these ions are covalent and have the definite lengths and spatial distributions that are characteristic of covalent bonds. The water-insoluble nonmolecular group of sulfur compounds is well represented by the heavy-metal sulfides such as mercuric sulfide. The atoms in these compounds are arranged in infinite chains, layer structures, or three-dimensional arrays and the interatomic bonds are largely covalent.

#### FINITE MOLECULAR COMPOUNDS

Since covalent bonds are directed bonds having a definite stereochemistry, it is possible to further classify the molecular compounds of sulfur according to the type, number, and angular distribution of the bonds that sulfur is able to form with the other atoms. Among the elements sulfur is unusually rich in this respect.

In the usual treatments of the comparative chemistry of sulfur compounds, it is the custom to discuss the energies of the various bonds separately or to regard the compounds as derivatives of the various sulfur acids or oxides wherever possible. These approaches unfortunately serve to mask the true relationships of these compounds. If, instead, we consider all the bonds formed by sulfur in a given molecule and consider their total energy and distribution, and account for the total number of valence electrons about the sulfur atom and the number of electrons contributed by the sulfur atom to its bonds, we obtain the classification shown in Table I. This scheme establishes a hierarchy of sulfur compounds as regards the key qualities of energy level and stability. There are a large number of organic covalent sulfur compound types known, of which only a small number have been included in Table I. So far as is known, however, the sulfur atom bonds in these generally more complex molecules conform to one or more of the structural types of sulfur shown in Table I.

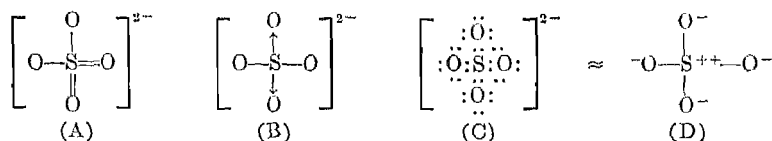
The sulfur atom can be pictured here as existing in a sequence of electronic states, each having a definite configuration (directed covalent bonds) and requiring a definite energy to attain the particular state. At one extreme this energy is supplied thermally and at the other it is supplied by the chemical environment (fluorine, oxygen, etc.). Each of these states of sulfur defines a class of covalent molecular compounds of sulfur containing one or more members. The successive states, going down the table, represent diminishing energy levels for the sulfur atom in the corresponding class of compound. Stability against environmental (chemical) influences tends to increase going down the table, but thermal stability in general decreases.

The representations of the sulfur atom in Table I are purely formal. The dots represent nonbonding electrons, and each line represents an electron pair bond in which one of the electrons is supplied by the sulfur. An arrow denotes an electron-pair bond in which both electrons are supplied by the sulfur. Formal bond representations are not always adequate to describe simply or accurately the actual valence



state of an atom or the character of its bonds in certain compounds. This is particularly true of the bond formed between sulfur and oxygen in all of the polyatomic compounds of sulfur. These bonds are given alternative representation in Table I as either dative (also termed semipolar or coordinate covalent) single bonds, indicated by arrows, or as conventional double bonds. These represent two limiting types of bonds involving eight and ten (or twelve) valence electrons, respectively, about the sulfur atom. In the early or classical formulations of valence bonds, the double bond was used between sulfur and oxygen, but this was later replaced by the dative single bond on the basis of certain stereochemical considerations.

For the sulfate ion, for example, the older conventional double-bond formula (A) or the dative-bond formula (B) must be understood as representing only two of many possible resonating hybrids. Formulas (C) and (D) are more precise descriptions of

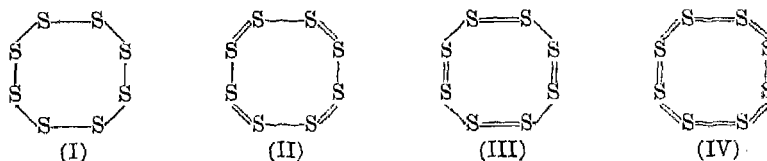


the electronic structure in that they emphasize the equivalence of the four oxygen atoms. Similarly, in other ions such as the sulfite,  $\text{SO}_3^{2-}$ , sulfonate,  $\text{RSO}_3^-$ , and sulfinate,  $\text{RSO}_2^-$ , ions, the oxygen atoms are equivalent.

In recent years, considerable evidence has accumulated (2,6,10,14,19) that the S—O bond represents contributions from both the dative single and conventional double forms, and many properties and reactions of sulfur compounds have been explained on this basis (17). Both experimental data and theoretical considerations (9,10) indicate that double bonds formed by contribution of a pair of electrons by the oxygen atom make the major contribution, particularly in the tetrahedral group of compounds.

Similar double bonding with an expanded valence shell in the sulfur can be expected between sulfur and nitrogen, and this is undoubtedly the case in the sulfines (sulfilimines). There is also good reason to suppose that S—S bonds in compounds such as rhombic and chain sulfur and in sulfides and halides of the types  $\text{R}_2\text{S}_n$  and  $\text{S}_n\text{X}_2$  have a significant degree of multiple bond character. The sulfur chains in these compounds ideally meet the requirements usually postulated for resonance. It has been suggested that such resonance forms in both ring and chain sulfur, involving expansion of the valence electron octet with formation of alternate double and single bonds, could account for the relative ease of breaking S—S bonds in the reactions of such compounds (13).

Thus, the  $\text{S}_8$  ring may be simply represented by the following four out of many possible resonance hybrids:



Forms (II) and (III) probably make major contributions. Two possible resonating forms of open-chain structures are:

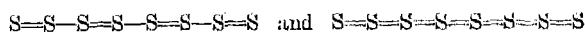


TABLE I. Classification of Covalent Sulfur Compounds.

Conventional (formal) model of S atom in compound	Examples	Spatial configuration of bonds about S atom	Total heat of formation of S bonds from atoms, $\Delta H$ , in kg.-cal./g.- atom S
$\begin{array}{c} \cdot\cdot \\ \text{S} \\ \cdot\cdot \end{array}$	S	Nonbonding, mono- atomic	0
$\begin{array}{c} \cdot\cdot \\ \text{S} - \\ \cdot\cdot \end{array}$	S <sub>2</sub> , SO	Diatomic, paramag- netic	102-116
$\begin{array}{c} \cdot\cdot \\ =\text{S} \\ \cdot\cdot \end{array}$	CS <sub>2</sub> , COS R <sub>2</sub> CS (thiones) RCHS (thials)	Terminal S	126
$\begin{array}{c} \cdot\cdot \\ -\text{S}- \\ \cdot\cdot \end{array}$	S <sub>8</sub> rhombic (also monoclinic and liquid S below 160°C)	Closed ring, 106° angle bonds	127
$\begin{array}{c} \cdot\cdot \\ -\text{S}- \\ \cdot\cdot \end{array}$	S <sub>4</sub> , S <sub>6</sub> , S <sub>n</sub> (viscous S, plastic S, insoluble S) SCl <sub>2</sub> , S <sub>2</sub> Cl <sub>2</sub> , S <sub>2</sub> Br <sub>2</sub> , S <sub>n</sub> X <sub>2</sub> R <sub>2</sub> S, R <sub>2</sub> S <sub>2</sub> , R <sub>2</sub> S <sub>n</sub>	Open chains, 106° angle bonds	130-133
$\begin{array}{c} \cdot\cdot \\ -\text{S}- \\ \cdot\cdot \end{array}$	H <sub>2</sub> S	90° angle	173
$\begin{array}{c} \uparrow \\ -\text{S}- \text{ or } -\text{S}- \\ \cdot\cdot \quad \parallel \end{array}$	SOCl <sub>2</sub> , SOF <sub>2</sub> , R <sub>2</sub> SO (sulfoxides) RSOOH (sulfinic acids) RSOOR (sulfinic esters) ROSOOH (alkyl bisulfites) ROSOOR (alkyl sulfites) R <sub>2</sub> SNR (sulfinimes)	Trigonal pyramidal	233
$\begin{array}{c} \cdot\cdot \\ =\text{S} \rightarrow \text{ or } =\text{S} = \\ \cdot\cdot \end{array}$	SO <sub>2</sub>	120° angle	252
$\begin{array}{c} \uparrow \\ -\text{S}- \text{ or } -\text{S}- \\ \downarrow \quad \parallel \end{array}$	SO <sub>2</sub> Cl <sub>2</sub> , H <sub>2</sub> SO <sub>4</sub> R <sub>2</sub> SO <sub>2</sub> (sulfones) RSO <sub>3</sub> OH (sulfonic acids) ROSO <sub>3</sub> OH (alkyl bisulfates) ROSO <sub>3</sub> OR (alkyl sulfates)	Tetrahedral	324
$\begin{array}{c} \uparrow \\ =\text{S} \rightarrow \text{ or } =\text{S} = \\ \diagdown \quad \diagup \end{array}$	SO <sub>2</sub>	Sym. planar	333
$\begin{array}{c} \diagup \quad \diagdown \\ \text{S} \\ \diagdown \quad \diagup \end{array}$	SF <sub>6</sub> , S <sub>2</sub> F <sub>10</sub>	Octahedral	421-428

Hydrogen, which is often anomalous in its behavior, provides no exception with sulfur. The evidence is that it forms right-angled *pp* orbital bonds in place of the obtuse-angled *sp* orbital bonds preferentially formed between sulfur and all but the most electronegative elements. There is some doubt as to the proper classification of the various sulfur compounds, other than hydrogen sulfide, which contain S—H bonds. It is probable that RSSH, HSSH, and H<sub>2</sub>S<sub>n</sub> belong to the obtuse-angled classification. Whether the mercaptans, RSH, are to be classified with hydrogen sulfide or with the obtuse-angled group is uncertain at the present time. Certain unsymmetrically substituted sulfoxides, sulfinimes, and sulfinic esters have been resolved into optically active enantiomorphs. This is in conformity with the assignment of pyramidal structures to these molecules. The resonance properties of sulfur are such that certain heterocyclic organic molecules such as thiophenes and thianaphthenes display a considerable degree of aromatic character.

Nitrogen and phosphorus compounds of sulfur have not been included in this summary because of the lack of adequate thermodynamic and structural data regarding them. It may be noted, however, that sulfur nitride, S<sub>4</sub>N<sub>4</sub>, is believed to form an

eight-membered ring structure with alternating S and N atoms, while sulfamide,  $(\text{NH}_2)_2\text{SO}_2$ , is undoubtedly tetrahedral in structure. Sulfimide,  $(\text{SO}_2\text{NH})_3$ , however, appears to have a cyclic structure, while imidodisulfamide,  $\text{NH}(\text{SO}_2\text{NH}_2)_2$ , has a chain structure and also forms still longer chains,  $\text{NH}_2\text{SO}_2(\text{NHSO}_2)_n\text{NH}_2$  (22).

The crystals formed by molecular compounds of sulfur in the solid state are held together by weak van der Waals forces. They are characteristically soft, low melting, and low boiling. The relatively high heat of sublimation, over 20 kg.-cal./mole, for rhombic sulfur, as against values under 10 kg.-cal./mole for typical van der Waals solids, appears at first sight to be inconsistent with this picture. The explanation lies in the simultaneous separation of the  $\text{S}_8$  molecules and the rupture of S—S bonds in a fraction of the ring molecules to form chains. Hydrogen bonding and hydrate formation are relatively unimportant among the molecular compounds of sulfur because of their nonionic character and the relatively low electronegativity of sulfur.

The angles formed between bonds in sulfur compounds are indicated in a general way in Table I. Some distortion from typical or normal bond angles occurs in some sulfur compounds particularly among the tetrahedral group. Bond angles and dihedral angles for particular compounds may be found in references (11,21,22). Structure determinations by physical methods and much of the chemical evidence have proved the presence of linear (unbranched) chains rather than branched chain structures for some polythionates and polysulfides (7).

The energy of formation of all the bonds about the sulfur atom is shown in the last column of Table I for the various classes of molecular sulfur compounds. Individual bond energies are of doubtful value in any general discussion of the structure and properties of sulfur compounds. This is due to the fact that individual bond energies are generally derived from particular reactions which often involve more than one bond in the molecule. This subjects them to interpretation and limits their usefulness. Thus, in the case of the S—S bond, there is evidence that although the average bond energy is found to 63.8 kg.-cal. from the heat of formation of  $\text{S}_8$  ring sulfur, the actual bond energy in all S—S bond reactions, short of the splitting of diatomic sulfur, is about 30 kg.-cal. (4,13). Calculation of bond energies from thermochemical data for the equilibrium of gaseous sulfur species and for the  $\text{S}_2\text{F}_{10}$  molecule also indicate values close to 30 kg.-cal.

Recent studies of the equilibrium of molecular species in sulfur vapor are of particular interest in that they establish the existence of  $\text{S}_4$  chain molecules in the vapor between about 500 and 800°C. The almost universal postulation of  $\text{S}_2$ ,  $\text{S}_6$ , and  $\text{S}_8$  as the sole molecules (plus S at very high temperatures) in the vapor has been based on the fact that the assumption of these species alone best fitted equilibrium measurements made shortly after the turn of the century. Two sets of more recent determinations have failed to agree with these earlier measurements and the assumption of  $\text{S}_4$  as an additional molecular species is necessary to account for the observed data (3). Thermochemical and other considerations exclude the existence of odd-numbered molecules in significant quantities, and the same consideration suggest that the vapor molecules must be chains, except at low or moderate temperatures, as over liquid sulfur, where  $\text{S}_8$  rings predominate in the vapor.

The lengths of bonds formed between sulfur and other elements in its molecular compounds are shown in Table II. The use of single lines to denote the bond does not mean that the bond is single. In fact, all of these bonds are believed to have some degree of multiple bond character with the exception of S—F, S—C (where S is not terminal), S—H, and the S—S bond in  $\text{S}_2\text{F}_{10}$ . The double line is used here to denote

TABLE II. Covalent Bond Lengths in Molecular Sulfur Compounds.

Bond	Occurrence	Bond length, A.
S—F	SF <sub>6</sub> , S <sub>2</sub> F <sub>10</sub> , SO <sub>2</sub> F <sub>2</sub>	1.58
S—Cl	S <sub>2</sub> Cl <sub>2</sub> , SCl <sub>2</sub> , SO <sub>2</sub> Cl <sub>2</sub> , SOCl <sub>2</sub>	1.99
S—Br	S <sub>2</sub> Br <sub>2</sub> , SOBr <sub>2</sub>	2.27
S—C	RSH, R <sub>2</sub> S	1.82
S=C	CS <sub>2</sub> , COS, R <sub>2</sub> CS	1.55
S=P	PSF <sub>3</sub> , P <sub>4</sub> O <sub>6</sub> S <sub>4</sub>	1.85
S—H	H <sub>2</sub> S	1.35
S—O	SO <sub>2</sub> , SO <sub>3</sub> , SOCl <sub>2</sub> , SO <sub>2</sub> Cl <sub>2</sub> , SOF <sub>2</sub> , SO <sub>2</sub> Br <sub>2</sub>	1.43
S—S	S <sub>n</sub> (s), S(l), S(g), S(plastic), S <sub>2</sub> Cl <sub>2</sub> , H <sub>2</sub> S <sub>2</sub>	2.08
S—S	S <sub>2</sub> F <sub>10</sub>	2.3
S=S	S <sub>2</sub>	1.92

a terminal sulfur atom in the molecule. Comparison with theoretical single- and double-bond lengths is not shown here, since the assignment of such lengths involves assumptions which have not held up too well in the case of sulfur bonds.

The S—S bond in S<sub>2</sub>F<sub>10</sub> is particularly interesting as the sole example of a true single sulfur—sulfur bond. Five of the six valence electrons in each of the sulfur atoms are promoted to bonding electrons by the fluorine, leaving only one electron to each sulfur for the formation of a single-electron-pair covalent bond between the sulfur atoms. The bond length of 2.3 Å. conforms with this view. The other S—S bonds at 2.1 Å. have some multiple-bond character through the utilization of available *d* orbitals as described above. Diatomic sulfur, like diatomic oxygen, is paramagnetic and presumably contains a multiple bond characterized by two unpaired electrons. The constancy of the S—O bond in many sulfur compounds despite the differences in bond energies and multiple bond character required of them is an outstanding difficulty of modern electron bond theory as applied to sulfur bonds (20).

#### HIGH POLYMERIC COMPOUNDS

This group of sulfur compounds comprises the polymeric molecules of insoluble sulfur, solid sulfur trioxide, the higher polythionic acids, and the higher polysulfides. The last include the higher alkali polysulfide salts, the higher hydrogen polysulfides, the polyalkylene polysulfides, and the longer-chain sulfur chlorides.

Insoluble sulfur occurs as a metastable, true high polymer, containing many thousands of sulfur atoms, in both plastic and crystalline forms. The chains are believed to have a seven-atom two-turn spiral as the repeating structural unit (11). There is considerable evidence that the long sulfur chains are terminated by non-sulfur atoms and radicals, representing very small percentages of impurities (1). The "insoluble sulfur" formed by precipitation from aqueous solutions of sulfur acids is presumably long-chain polythionic acids. The high solubility and deep color of sulfur in alkalis suggests the existence of long-sulfur-chain anions. The properties of liquid sulfur treated with chlorine or hydrogen sulfide indicate the existence of long-chain polysulfides of chlorine or hydrogen (13), and polysulfides up to chain lengths in the hundreds have been reported (5). Characteristically, all of the inorganic sulfur compounds of this group are unstable or metastable at low or moderate temperatures and are invariably polydisperse, that is, they are of mixed chain length or molecular weight.

High-molecular polyalkylene polysulfides, R[S<sub>m</sub>(CH<sub>2</sub>)<sub>n</sub>]<sub>x</sub>R, also belong to this group of high polymeric compounds. These polymers are considerably more stable

than the inorganic group of high polymers. The sulfur is believed to occur as linear chains, containing from about 2 to 4 sulfur atoms per unit. Molecular weights run to large values in the higher members of this series which have rubberlike properties.

#### NONMOLECULAR COMPOUNDS

**Water-Soluble Ionic Compounds.** This group is represented by the salts of the sulfur oxygen acids, by the sulfides, polysulfides, and hydrosulfides of the alkali and alkaline earth metals, and by the sulfonium cation salts. The pure or solid forms of these compounds are in the main typical, largely ionic crystals in which the arrangement of the ions in the infinite crystal lattice is determined by geometrical considerations. The crystals are characteristically hard and high-melting. Hydrates are common in this group, and hydrogen bonding is frequently encountered. The occurrence of a compound as ions in solution does not imply the necessary occurrence of ionic bonds in the pure compound. The sulfur oxygen acids, wherever they occur in pure form, are notable examples in that they are molecular covalent compounds which form ions in aqueous solution.

As remarked above, the ionic compounds of sulfur are chiefly of interest in aqueous solution, where the various ions can be regarded as charged molecules. This is justified by the fact that the bonds within these ions are covalent bonds with angles and lengths the same or very nearly so as in the molecular compounds of sulfur. In all of its polyatomic ions, sulfur adopts one of four configurations with respect to the number and distribution of its bonds (see Table III).

TABLE III. Ionic Structural Types Containing Sulfur.

Configuration	Examples
Terminal	$S_2^{2-}$ , the thio sulfur atom in $S_2O_3^{2-}$ , $CNS^-$
Angular chain (about $103^\circ$ )	$S_2^{2-}$
Trigonal pyramidal	$SO_3^{2-}$ , $R_3S^+$ , $HSO_3^-$
Tetrahedral	$SO_4^{2-}$ , $HSO_4^-$ , $SO_3F^-$ , $SO_3NH_2$

Most of the complex sulfur ions, including the polythionates, polysulfides, pyrosulfites (metabisulfites), pyrosulfate, and peroxyacid ions contain one or more of the types of sulfur atom shown in Table III. The ion  $S_2^{2-}$  and its derivative  $HS^-$  complete the roster of sulfur ion types of known structure. (Sulfoxylate and dithionite ions are also known, but their configurations have not been established (see below)).

The four sulfur types in Table III are analogous to four of the sulfur types given in Table I. They also possess the same relative order of stabilities and energy levels. The analogy cannot, however, be carried any further. The various sulfur ions exist at somewhat lower energy levels and are more stable than their corresponding nonionic types. The corresponding bond lengths in the ions also appear to be somewhat longer. There does not appear to be a theoretical treatment of orbitals in ions at the present time that can satisfactorily account for the observed structures.

The organic sulfonium ion,  $R_3S^+$ , is well known and its pyramidal structure is established by its optical activity when the three organic substituents are different. Not so well established is the "inorganic sulfonium ion,"  $SCl_3^+$ . This ion undoubtedly occurs in the compound  $SCl_4$ , which differs in many ways from the other, covalent sulfur chlorides;  $SCl_4$  is known only in the solid state at low temperatures and has a relatively high dielectric constant characteristic of a salt structure (15,18). Sulfur oxytetrachloride,  $S_2O_3Cl_4$ , is also believed to have a salt structure  $[SCl_3]^+ [ClSO_3]^-$  (18). Since chlorine can replace alkyl carbon in covalent sulfur compounds without change

in the energy and distribution of the sulfur bonds (see Table I), it can be presumed that the inorganic sulfonium ion has a pyramidal structure like its organic analogs.

The salts of the sulfur oxygen acids are by far the most numerous and important members of the soluble ionic group of sulfur compounds. The structures, existence, and stabilities of these compounds are summarized in Table IV. The ions are listed according to their parent acids in order of increasing oxygen content, except for the polythionate, which best follows the dithionate ion for structural reasons.

As indicated above, all of these structures can be taken to be combinations of the sulfur-containing ion types shown in Table III, and most of these structures have been established by x-ray studies (21) backed by strong chemical and physical-chemical evidence. The only structure, in fact, that is not well established is that of the dithionite ion. The structure given in Table IV is preferred as being consistent with the general structural behavior of sulfur and is supported by Raman spectra data (16). The alternate structure sometimes proposed involves linkage of the sulfurs through one oxygen atom and is based solely on interpretations of chemical behavior. Such evidence is rather unconvincing, however, if the chemical behavior and proved structure of other oxysulfur anions are similarly considered.

TABLE IV. Oxygen Acids of Sulfur and Their Salts.

Formula	Name	Structure	Acid <sup>a</sup>		Salts <sup>a</sup>	
			Pure	In soln.	Pure	In soln.
H <sub>2</sub> SO <sub>2</sub>	Sulfoxylic	O—S—O <sup>2-</sup>	—	—	?	?
H <sub>2</sub> S <sub>2</sub> O <sub>3</sub>	Thiosulfuric	S—SO <sub>3</sub> <sup>2-</sup>	—	?	+	+
H <sub>2</sub> S <sub>2</sub> O <sub>4</sub>	Dithionous (hydrosulfurous)	O <sub>2</sub> S—SO <sub>2</sub> <sup>2-</sup>	—	+*	+	+*
H <sub>2</sub> S <sub>2</sub> O <sub>5</sub>	Pyrosulfurous	O <sub>2</sub> S—SO <sub>3</sub> <sup>2-</sup>	—	?	+	+
H <sub>2</sub> SO <sub>3</sub>	Sulfurous	SO <sub>3</sub> <sup>2-</sup>	—	+	+	+
H <sub>2</sub> S <sub>2</sub> O <sub>6</sub>	Dithionic	O <sub>3</sub> S—SO <sub>3</sub> <sup>2-</sup>	—	+	+	+
H <sub>2</sub> S <sub>4</sub> O <sub>6</sub>	Polythionic	O <sub>3</sub> S—S—SO <sub>3</sub> <sup>2-</sup>	—	+	+	+
H <sub>2</sub> S <sub>2</sub> O <sub>7</sub>	Pyrosulfuric	O <sub>3</sub> S—O—SO <sub>3</sub> <sup>2-</sup>	+*	—	+	—
H <sub>2</sub> SO <sub>4</sub>	Sulfuric	SO <sub>4</sub> <sup>2-</sup>	+*	+	+	+
H <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	Peroxydisulfuric	O <sub>3</sub> S—O <sub>2</sub> —SO <sub>3</sub> <sup>2-</sup>	+	+*	+	+
H <sub>2</sub> SO <sub>5</sub>	Peroxymonosulfuric	O <sub>3</sub> S—O—O <sup>2-</sup>	+	+*	—	?

<sup>a</sup> + exists, — not known, ? uncertain existence, \* unstable.

**Insoluble Crystal-Lattice Compounds.** This group of sulfur compounds is represented almost exclusively by the water-insoluble sulfides of the metals and the semimetallic elements. Some of the most insoluble of all inorganic compounds are found among the heavy-metal sulfides. The atoms in these nonmolecular compounds are arranged in infinite chains, layers, or three-dimensional arrays, and the interatomic bonds are largely covalent. This interesting group is partly classified as shown in Table V (21). Some of the sulfides appear under two or more structural types because of transitions at certain temperatures. The soluble alkali sulfides and the alkaline earth sulfides, which are not shown here, have the antifuorite and rock salt type of structures, respectively.

Low melting points, glassy structures, and fibrous needles are typically found among the infinite-chain-type sulfides. Some are rapidly and completely hydrolyzed by water. The layer-structure sulfides exhibit characteristic lubricant and leafing pigment properties. Molybdenum sulfide, strongly resembling graphite, and stannic sulfide, which forms golden yellow leaflets known as mosaic gold, are typical. The

TABLE V. Structural Classification of Metal Sulfides.

- 
- |                                      |                                                                                                        |
|--------------------------------------|--------------------------------------------------------------------------------------------------------|
| A. Infinite chains.                  | $\text{Sb}_2\text{S}_3$ , $\text{Bi}_2\text{S}_3$ , $\text{SiS}_2$                                     |
| B. Infinite layers.                  |                                                                                                        |
| 1. Molybdenite type:                 | $\text{MoS}_2$ , $\text{WS}_2$                                                                         |
| 2. Cadmium iodide type:              | $\text{TiS}_2$ , $\text{ZrS}_2$ , $\text{SnS}_2$ , $\text{PtS}_2$                                      |
| 3. Complex layer:                    | $\text{CuS}$ , $\text{CuSbS}_2$                                                                        |
| C. Infinite 3-dimensional complexes. |                                                                                                        |
| 1. Antifluorite type:                | $\text{Cu}_2\text{S}$                                                                                  |
| 2. Rock salt type:                   | $\text{MgS}$ , $\text{MnS}$ , $\text{PbS}$                                                             |
| 3. Nickel arsenide type:             | $\text{FeS}$ , $\text{CoS}$ , $\text{NiS}$ , $\text{VS}$                                               |
| 4. Pyrite or marcasite type:         | $\text{FeS}_2$ , $\text{CoS}_2$ , $\text{NiS}_2$ , $\text{MnS}_2$ , $\text{OsS}_2$ , $\text{RuS}_2$    |
| 5. Zinc blende type:                 | $\text{ZnS}$ , $\text{CdS}$ , $\text{MnS}$ , $\text{BeS}$ , $\text{HgS}$                               |
| 6. Wurtzite type:                    | $\text{ZnS}$ , $\text{CdS}$ , $\text{MnS}$                                                             |
| 7. Miscellaneous types:              | $\text{PtS}$ , $\text{PdS}$ , $\text{NiS}$ , $\text{SnS}$ , $\text{HgS}$ , $\text{GeS}$ , $\text{GeS}$ |
- 

bulk of the metal sulfides are to be found in the infinite three-dimensional group. For the most part these crystals are colored, high-melting, and moderately hard. Many heavy-metal sulfides have a metallic appearance and metallic properties. Some of these sulfides form defect structures of several types, leading to unusual properties such as electrical conductance, fluorescence, and nonstoichiometric proportions. Because of their ability to form structures of varying proportions and the ability to substitute other atoms in the crystal lattice, a literally endless variety of metal sulfides and related compounds are capable of existence.

Among the sulfides of unknown structure,  $\text{B}_2\text{S}_3$  and  $\text{SiS}$  probably have chain structures, while  $\text{V}_2\text{S}_3$  and  $\text{Cr}_2\text{S}_3$  are probably of the layered structure type.

### Bibliography

- (1) Bacon, R. F., and Fanelli, R., *J. Am. Chem. Soc.*, **65**, 639 (1943).
- (2) Barnard, D., Fabian, J. M., and Koch, H. P., *J. Chem. Soc.*, **1949**, 2442-54.
- (3) Braune, H., Peter, S., and Neveling, V., *Z. Naturforsch.*, **62**, 32-37 (1951).
- (4) Cooley, R. A., and Yost, D. M., *J. Am. Chem. Soc.*, **62**, 2474 (1940).
- (4a) Faessler, A., and Goehring, M., *Naturwissenschaften*, **39**, 167-77 (1952).
- (5) Feher, F., *et al.*, *Z. Naturforsch.*, **B7**, 574-75 (1952).
- (6) Fehnel, E. A., and Carmack, M., *J. Am. Chem. Soc.*, **71**, 84, 231, 2889 (1949).
- (7) Foss, O., *Acta Chem. Scand.*, **4**, 404 (1950).
- (8) Kelley, K. K., *U.S. Bur. Mines, Bull.*, **406**, (1937).
- (9) Moffitt, W. E., *Proc. Roy. Soc.*, **A200**, 409 (1950).
- (10) Palmer, K. J., *J. Am. Chem. Soc.*, **60**, 2360 (1938).
- (11) Pauling, L., *Proc. Natl. Acad. Sci. U.S.*, **35**, 495 (1949).
- (12) Pauling, L., *The Nature of the Chemical Bond*, 2nd ed., Cornell Univ. Press, Ithaca, N.Y., 1944.
- (13) Powell, R. E., and Eyring, H., *J. Am. Chem. Soc.*, **65**, 648 (1943).
- (14) Rothstein, E., *J. Chem. Soc.*, **1940**, 1950.
- (15) Sidgwick, N. V., *The Chemical Elements and Their Compounds*, Vol. II, pp. 875-947, Clarendon Press, Oxford Univ., 1950.
- (16) Simon, A., and Küchler, H., *Z. anorg. Chem.*, **260**, 161-84 (1949).
- (17) Tarbell, D. S., and Harnish, D. P., *Chem. Revs.*, **49**, No. 1 (1951).
- (18) Thorne, P. C. L., and Roberts, E. R., *Inorganic Chemistry (Ephraim)*, 4th ed., rev., Nordeman, N.Y., 1943.
- (19) Wheland, G. W., *Advanced Organic Chemistry*, 2nd ed., Wiley, N.Y., 1949, pp. 355-61.
- (20) Wells, A. F., *J. Chem. Soc.*, **1949**, 55.
- (21) Wells, A. F., *Structural Inorganic Chemistry*, 2nd ed., Clarendon Press, Oxford Univ., 1950, pp. 318-58, 392-407.
- (22) Yost, D. M., and Russell, H., *Systematic Inorganic Chemistry*, Prentice-Hall, N.Y., 1944.

PAT MACALUSO

**SULFUR COMPOUNDS, INORGANIC**

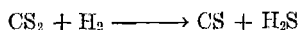
In this article the inorganic compounds of sulfur with most of the nonmetals will be discussed. The sulfides, sulfates, and sulfites of the metals are generally described under such headings as: *Iron compounds*; *Lead compounds, inorganic*; *Magnesium compounds*. For other inorganic sulfur compounds see: *Chlorosulfonic acid*; *Fluorine compounds, inorganic*; *Peroxides and peroxy compounds, inorganic*; *Phosphorus compounds, inorganic*; *Silicon compounds, inorganic*; *Sulfamic acid*; *Sulfuric acid*; *Thio acids*; *Thionic acids*; *Thiosulfuric acid*; *Xanthic acids*.

**Carbon Sulfides and Derivatives.**

Sulfur and carbon combine to form a number of compounds including carbon subsulfide,  $C_3S_2$ ; carbon monosulfide,  $CS$ ; and the well known carbon disulfide,  $CS_2$ . Also reported, although of somewhat less certain existence, are  $C_4S$ ,  $C_6S_2$ , and  $C_2S_3$ . A vast system of derivatives of the carbon sulfides exists. However, since these shade off into organic chemistry, only the oxygen and chlorine derivatives will be considered here.

**Carbon subsulfide**,  $C_3S_2$ , formula weight 100.16, is a deep red lacrimatory liquid produced by the action of an electric arc on carbon disulfide. It reacts with bromine to produce a compound of the composition  $C_3S_2Br_6$ .

**Carbon monosulfide**,  $CS$ , formula weight 44.08, is an unstable gas produced by the reduction of carbon disulfide by either hydrogen or carbon monoxide in the presence of a silent electrical discharge:



Its life at room temperature is about 10 minutes, while at  $100^\circ C$ . it is only 3 minutes. It is detected by its absorption spectrum.

**Carbon disulfide**,  $CS_2$ . See Vol. 3, p. 142.

**Carbonyl sulfide** (carbon oxysulfide),  $COS$ , formula weight 60.08, is a colorless and odorless gas, m.p.  $-138.2^\circ C$ .; b.p.  $-50.2^\circ C$ .; crit. temp.  $105^\circ C$ .; crit. pressure 60.5 atm.; densities, of solid, 1.52 at  $-195^\circ C$ ., of liquid, 1.24 at  $-87^\circ C$ . Its heat of fusion is 18.81 cal./gram at  $-138.2^\circ C$ .; heat of vaporization 73.62 cal./gram at  $-50.2^\circ C$ .; heat of formation 545.98 cal./gram for gas at  $25^\circ C$ .; free energy of formation  $-673.31$  cal./gram for gas at  $25^\circ C$ . The specific heat for the gas between 25 and  $1500^\circ C$ . is given by the equation:

$$C_p \text{ (cal./mole)} = 12.89 + 0.83 \times 10^{-3}T - 3.60 \times 10^{-5}T^{-2} \quad (T = ^\circ K.)$$

Concentrations between 11.9 and 28.5% of carbonyl sulfide in air are explosive. The vapor pressure of carbonyl sulfide at various temperatures is as follows:

Temperature, $^\circ C$ .....	-40	-30	-20	-10	0	10	20	30	40	50	60
Vapor pressure, atm.....	1.5	2.2	3.1	4.4	6.1	8.2	11.4	15	18	22	27

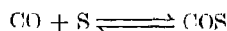
The solubility in water at various temperatures is:

Temperature, $^\circ C$ .....	0	5	10	15	20	25	30
Solubility, g. per 100 ml. $H_2O$							
per atm. partial pressure...	0.356	0.281	0.221	0.179	0.147	0.122	0.104

1.7 g. of carbonyl sulfide dissolves in 100 ml. of alcohol and 3.2 g. in 100 ml. of toluene at  $22^\circ C$ . Its dipole moment is  $0.650 \times 10^{-18}$  c.g.s. unit.



Carbonyl sulfide is always formed when carbon, oxygen, and sulfur or their compounds such as carbon monoxide, carbon disulfide, and sulfur dioxide are brought together at high temperatures. Hence, carbonyl sulfide is found as an impurity in various types of manufactured gases and as a by-product in the manufacture of carbon disulfide. Carbonyl sulfide in these reactions is produced basically by the reaction:



This reaction, when catalyzed with kaolin for example, proceeds to the right at temperatures up to about 500°C. At higher temperatures the equilibrium tends toward the left, the carbonyl sulfide being 64% dissociated at 900°C.

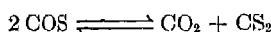
Carbonyl sulfide may be prepared by a number of other reactions, some of which are listed in Table I.

TABLE I. Some Reactions Yielding Carbonyl Sulfide.

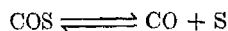
Reaction	Condition
$\text{CO}_2 + \text{CS}_2 \rightleftharpoons 2 \text{COS}$	About 500°C.; quartz catalyst
$\text{CS}_2 + 3 \text{SO}_2 \rightarrow \text{COS} + 4 \text{SO}_2$	React in oleum at about 100°C.
$\text{ROCSOK} + \text{HCl} \rightarrow \text{COS} + \text{ROH} + \text{KCl}$	—
$\text{COCl}_2 + \text{CdS} \rightarrow \text{COS} + \text{CdCl}_2$	270°C.
$\text{HCNS} + \text{H}_2\text{O} \rightarrow \text{COS} + \text{NH}_3$	In conc. $\text{H}_2\text{SO}_4$ at 20°C.
$\text{NH}_2\text{COSNH}_2 + 2 \text{HCl} \rightarrow \text{COS} + 2 \text{NH}_4\text{Cl}$	—

Inasmuch as carbonyl sulfide reacts only slowly with aqueous alkali-metal hydroxides, these solutions may be used in removing acidic gases in the purification of this material.

Dry carbonyl sulfide is a rather stable compound. At elevated temperatures, however, it decomposes according to the equations:

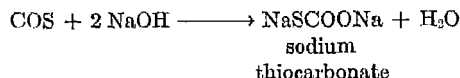


and



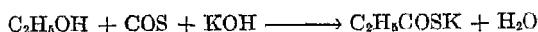
The first of these reactions predominates at temperatures around 600°C., and the second at temperatures around 900°C.

Carbonyl sulfide burns with a blue flame to carbon dioxide and sulfur dioxide. It is slowly hydrolyzed to carbon dioxide and hydrogen sulfide. It reacts slowly with aqueous alkali metal hydroxides to form thiocarbonates. These, however, are unstable, breaking down into carbonates and sulfides:



Carbonyl sulfide reacts with chlorine to form phosgene and sulfur dichloride. With ammonia, it forms urea and hydrogen sulfide.

Carbonyl sulfide reacts with alcohols in the presence of alkalies to form mono-thiocarbonates:



Its reaction with amines is somewhat similar:



**Thiophosgene** (thiocarbonyl chloride, carbon dichlorosulfide),  $\text{CSCl}_2$ , formula weight, 114.99, is a red liquid with a strong unpleasant odor: b.p.  $73.5^\circ\text{C}$ .;  $d_{20}^{15}$  1.5085.

It is produced by the reduction of trichloromethanesulfonyl chloride, either with hydrogen sulfide or with a metal plus an acid:



It may also be obtained by treating carbon tetrachloride at high temperatures with sulfur-containing reducing agents:



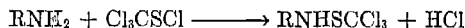
Other reducing agents used include iron sulfide, sulfur, and phosphorus sulfides.

Thiophosgene hydrolyzes to form carbon dioxide, hydrochloric acid, and hydrogen sulfide. It is readily chlorinated to trichloromethanesulfonyl chloride. When heated with sulfur at  $130\text{--}150^\circ\text{C}$ ., it forms  $\text{CS}_2\text{Cl}_2$ .

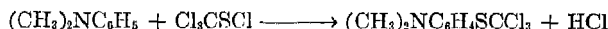
**Trichloromethanesulfonyl chloride** (perchloromethyl mercaptan),  $\text{Cl}_3\text{CSOCl}$ , formula weight 185.9, is a pale yellow oily liquid, b.p.  $149^\circ\text{C}$ . at 760 mm.,  $68^\circ\text{C}$ . at 52 mm.;  $d_{20}^{20}$  1.700;  $n_D^{24}$  1.538; surface tension 35.02 dynes/cm. at  $20^\circ\text{C}$ . It is insoluble in water but soluble in organic liquids.

Perchloromethyl mercaptan is stable at room temperature, but begins to decompose at its boiling point, sulfur chloride being among the decomposition products. It is hydrolyzed only slowly at room temperature; thiophosgene and trichloromethanesulfonyl chloride,  $\text{Cl}_3\text{CSO}_2\text{Cl}$ , are the primary hydrolysis products under these conditions. At  $160^\circ\text{C}$ ., the hydrolysis is rapid, carbon dioxide, hydrochloric acid, and sulfur being formed. At ordinary temperatures, metallic iron decomposes perchloromethyl mercaptan with the formation of carbon tetrachloride. Under some circumstances, however, iron may be used to reduce  $\text{CSCl}_4$  to thiophosgene. Oxidation of perchloromethyl mercaptan with nitric acid in acetic acid yields trichloromethanesulfonyl chloride, a solid that melts at  $140\text{--}142.5^\circ\text{C}$ . and resists hydrolysis. Treatment of  $\text{CSCl}_4$  with powdered silver yields bis(trichloromethyl) disulfide,  $(\text{CCl}_3)_2\text{S}_2$ , a thick yellow oil.

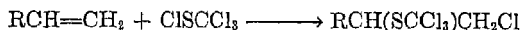
The organic reactions of  $\text{Cl}_3\text{CSOCl}$  are characterized by the reactivity of the chlorine on the sulfur atom. In its reaction with primary or secondary amines, amides, or imides, the nitrogen attaches to the sulfur:



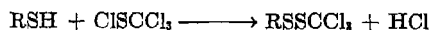
Dialkylarylamines when treated with perchloromethyl mercaptan give *p*-dialkylaminoaryl trichloromethyl sulfides. Thus with dimethylaniline the following reaction takes place:



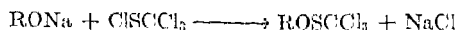
With olefins, perchloromethyl mercaptan reacts as follows:



In general, the thiol group ( $-\text{SH}$ ) is reactive toward perchloromethyl mercaptan:

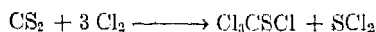


Correspondingly, the sodium alkoxides react:



An excess of sodium alkoxide produces the tetraalkyl ester of orthocarbonic acid.

Perchloromethyl mercaptan is prepared by the chlorination of carbon disulfide at 20°C. in the presence of iodine as a catalyst. The reaction is carried out batch-wise in glass-lined jacketed vessels, care being taken to exclude iron or other metals that would catalyze the formation of carbon tetrachloride. The reaction is:



The temperature of reaction is held low to prevent the formation of excess  $\text{S}_2\text{Cl}_2$ . It is difficult to separate  $\text{S}_2\text{Cl}_2$  by distillation. Chlorination is continued until 3–5% excess chlorine is present. A period of about 45 hours is required for the chlorination. The reaction mixture is then fractionally distilled under 20 in. vacuum to remove the  $\text{SCL}_2$ , excess chlorine, any unreacted carbon disulfide, and any carbon tetrachloride that may have been produced. Any  $\text{S}_2\text{Cl}_2$  present is difficult to remove by this means. An 85% yield of 97–98% purity is obtained.

The vapors of perchloromethyl mercaptan are extremely toxic, 1 p.p.m. being lethal to test animals during a three month exposure test. The material is also very corrosive to the skin. Accordingly, appropriate precautions must be taken in its handling, including the use of organic cartridge gas masks in contaminated areas. If perchloromethyl mercaptan is spilled on the skin, the area should immediately be flushed with water and washed thoroughly with soap and water.

Perchloromethyl mercaptan is an organic intermediate. It is used in the manufacture of the agricultural fungicide Captan, *N*-(trichloromethylthio)-4-cyclohexene-1,2-dicarboximide.

**Chlorosulfonic acid**,  $\text{HSO}_3\text{Cl}$ . See Vol. 3, p. 885.

## Hydrogen Sulfides.

Although more than one hydrogen sulfide is known, including hydrogen polysulfides, hydrogen sulfide,  $\text{H}_2\text{S}$ , is by far the best known and most important.

### Hydrogen Sulfide

Hydrogen sulfide (sulfuretted hydrogen, hydrosulfuric acid),  $\text{H}_2\text{S}$ , formula weight 34.08, is a colorless gas having an offensive odor. It occurs widely throughout nature and industry, mostly as an objectionable impurity. From it are produced substantial tonnages of elementary sulfur, sulfuric acid, and a variety of other chemicals.

Although its odor must have been recognized at a very early period, hydrogen sulfide was not described by the ancient Greek writers. The gas was first studied intensively by Scheele, who reported in 1777 that it could be obtained by the action of acids on calcium polysulfide, manganese sulfide, or ferrous sulfide. He also showed that it could be prepared by heating sulfur in hydrogen. Scheele observed the solubility of the gas in water and its oxidation to sulfur by air, nitric acid, or chlorine. He noted that the gas reacts with solutions of numerous metallic salts; however, it was not until it was analyzed by Berthollet in 1796 that the gas was recognized as hydrogen sulfide.

## PROPERTIES

M.p.  $-82.9^{\circ}\text{C}.$ ; b.p.  $-61.80^{\circ}\text{C}.$ ; sp. gr. of gas (air = 1.00) 1.189, of liquid  $d_4^{60}$  0.96;  $C_p$  between 25 and  $1500^{\circ}\text{C}.$   $0.236 + 9.74 \times 10^{-5}$  cal./gram ( $t = ^{\circ}\text{C}.$ ); heat of vaporization at  $-61.4^{\circ}\text{C}.$  131.9 cal./gram; heat of formation (gas,  $18^{\circ}\text{C}.$ )

TABLE II. Thermodynamic Properties of Hydrogen Sulfide.

Temp., $^{\circ}\text{K}.$	Entropy, $S^{\circ}$ , cal./deg. mole	Free energy, $-(F^{\circ} - H_0^{\circ})/T$ , cal./deg. mole	Heat content, $H^{\circ} - H_0^{\circ}$ , kg.-cal./mole	Heat capacity, $C_p^{\circ}$ , cal./deg. mole
298.16	49.15	41.18	2.38	8.14
400.	51.36	43.53	3.13	8.48
500.	53.30	45.34	3.99	8.81
600.	54.97	46.83	4.89	9.14
700.	56.40	48.13	5.82	9.47
800.	57.73	49.27	6.78	9.81
900.	58.96	50.30	7.78	10.14
1000.	59.81	51.24	8.81	10.47

154 cal./gram. The thermodynamic properties of hydrogen sulfide are given in Table II (2). See also references (24,35). Thermal conductivity 0.0076 B.t.u./(hr.) (sq.ft.) ( $^{\circ}\text{F}.$ /ft.) at  $32^{\circ}\text{F}.$  Vapor pressure:

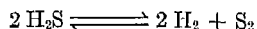
Temperature, $^{\circ}\text{C}.$ .....	0	10	20	30	40	50	60	70	80	90	100
Vapor pressure, atm.....	10.8	14.1	18.5	23.6	29.7	36.5	44.5	53.1	64.0	72.6	88.7

Crit. pressure 88.9 atm.; crit. temp.  $100.4^{\circ}\text{C}.$  Solubility in water:

Temp., $^{\circ}\text{C}.$ .....	0	10	20	30	40	50	60	70	80	90	100
Sol., g. per 100 g. soln. per atm. partial pressure	4.95	6.72	8.77	10.93	13.2	15.5	17.8	20.3	22.8	24.1	24.7

For solubility in amine solutions see reference (4); in alkali carbonates, bicarbonates, and hydrosulfides, reference (11); in liquid sulfur, reference (15); in hydrocarbon solvents, reference (29). Liquid hydrogen sulfide is generally a poor solvent for salts. It will, however, dissolve appreciable quantities of anhydrous aluminum halides,  $\text{ZnCl}_2$ ,  $\text{FeCl}_3$ ,  $\text{HgCl}_2$ ,  $\text{PCl}_3$ ,  $\text{SiCl}_4$ , and  $\text{SO}_2$ . Hydrogen sulfide has an ignition temperature of  $250^{\circ}\text{C}.$  and an explosive range in air of from 4.5 to 45.5%.

Although  $\text{H}_2\text{S}$  is thermodynamically stable at room temperature, at elevated temperatures it breaks down reversibly into its elements:



The equilibrium constant for this reaction at various temperatures is (24):

Temp., $^{\circ}\text{K}.$	$K = p^2(\text{H}_2)p(\text{S}_2)/p^2(\text{H}_2\text{S})$	Temp., $^{\circ}\text{K}.$	$K = p^2(\text{H}_2)p(\text{S}_2)/p^2(\text{H}_2\text{S})$
298.....	$1.7 \times 10^{-26}$	800.....	$2.2 \times 10^{-6}$
300.....	$2.7 \times 10^{-26}$	900.....	$4.3 \times 10^{-6}$
400.....	$7.6 \times 10^{-19}$	1000.....	$4.8 \times 10^{-5}$
500.....	$2.6 \times 10^{-14}$	1250.....	$3.8 \times 10^{-3}$
600.....	$2.9 \times 10^{-11}$	1500.....	$7.1 \times 10^{-2}$
700.....	$4.6 \times 10^{-9}$	1750.....	0.95

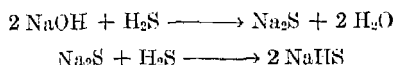
Hydrogen sulfide is readily oxidized by many oxidizing agents. The oxidation products depend upon the oxidizing agent, its concentration, and its molal ratio to the

hydrogen sulfide, and upon the conditions of the reaction. Some of the oxidizing agents for hydrogen sulfide and their products of oxidation are summarized in Table III. The reaction  $\text{H}_2\text{S} + \text{I}_2 \rightarrow 2\text{HI} + \text{S}$  is used in the analysis of hydrogen sulfide.

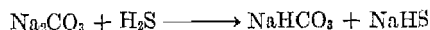
TABLE III. Oxidation of Hydrogen Sulfide.

Oxidizing agent	Conditions	Chief products
$\text{O}_2$ (air)	Flame. Air in excess	$\text{SO}_2$
$\text{O}_2$ (air)	Flame. $\text{H}_2\text{S}$ in excess	Sulfur
$\text{O}_2$ (air)	Aq. soln. of $\text{H}_2\text{S}$	Sulfur
$\text{SO}_2$	Elevated temp. plus catalyst	Sulfur
$\text{SO}_2$	Aq. soln.	Sulfur, polythionic acids
$\text{H}_2\text{SO}_4$	Concd. acid	Sulfur, $\text{SO}_2$
$\text{H}_2\text{O}_2$	Neutral soln.	Sulfur
$\text{H}_2\text{O}_2$	Alk. soln.	$\text{S}_2\text{O}_3^{2-}$ , $\text{SO}_4^{2-}$
$\text{Na}_2\text{O}_2$	Dry system at elevated temp.	$\text{Na}_2\text{S}$ , $\text{Na}_2\text{S}_x$
$\text{O}_3$	Aq. soln.	Sulfur, $\text{H}_2\text{SO}_4$
$\text{HNO}_3$	Concd. aq. soln.	$\text{H}_2\text{SO}_4$
$\text{NO}$	Silica gel catalyst	Sulfur
$\text{NO}_2^-$	pH 5-7	Sulfur, $\text{NO}$
$\text{NO}_2^-$	pH 8-9	Sulfur, $\text{NH}_3$
$\text{Cl}_2$	Gaseous reaction, excess $\text{Cl}_2$	$\text{SCl}_2$
$\text{Cl}_2$	Gaseous reaction, excess $\text{H}_2\text{S}$	Sulfur
$\text{Cl}_2$	Aq. soln., excess $\text{Cl}_2$	$\text{H}_2\text{SO}_4$
$\text{I}_2$	Aq. soln.	Sulfur
$\text{Fe}^{3+}$	Aq. soln.	Sulfur

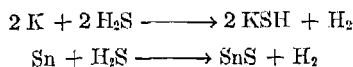
Completely dry hydrogen sulfide, whether gas or liquid, has no acidic properties. Aqueous solutions, however, are weakly acidic. The dissociation constant for the first hydrogen at  $18^\circ\text{C}$ . is  $9.1 \times 10^{-8}$  while that for the second hydrogen is  $1.2 \times 10^{-15}$ . A solution of hydrogen sulfide reacts with a wide variety of alkaline substances. Thus, it reacts with alkali-metal hydroxides to form first the normal sulfides and then the acid or hydrosulfides:



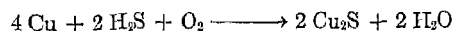
With alkali carbonates, however, the reaction proceeds only to the bicarbonate state, hydrogen sulfide being insufficiently acidic to release carbon dioxide from solution:



Alkali metals, when heated in hydrogen sulfide, react to form the acid sulfides, while tin and other metals form the normal sulfides:



Dry hydrogen sulfide does not react with metals such as mercury, silver, or copper, but in the presence of air and moisture the reaction is rapid:



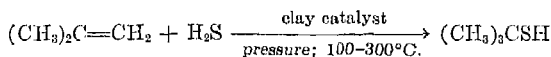
Hydrogen sulfide precipitates sulfides from many heavy-metal salt solutions. The solubility constants of these sulfides vary widely. Owing to the very small dissociation constant for the second hydrogen of hydrogen sulfide, the concentration of

sulfide ion in hydrogen sulfide solutions may be controlled over a broad range by adjustment of the pH. This control, in turn, permits the selective precipitation of heavy-metal sulfides. Such reactions are useful in the primary separation of the metals in the standard scheme of qualitative analysis.

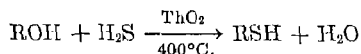
Hydrogen sulfide forms comparatively few addition compounds. At high pressures and low temperatures, it reacts with water to form the crystalline hydrate,  $\text{H}_2\text{S} \cdot 6\text{H}_2\text{O}$ . Aluminum bromide, either fused or in solution in carbon disulfide, will react with hydrogen sulfide to form the colorless crystalline compound  $\text{AlBr}_3 \cdot \text{H}_2\text{S}$ , m.p.  $83^\circ\text{C}$ . Correspondingly, boron trichloride reacts with liquid hydrogen sulfide to form the white crystalline compound  $\text{BCl}_3 \cdot 12\text{H}_2\text{S}$ .

Hydrogen sulfide appears to react with liquid sulfur at elevated temperatures to form long-chain hydrogen polysulfides. These markedly reduce the viscosity peak of liquid sulfur.

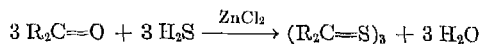
Hydrogen sulfide reacts with olefins at elevated temperatures and pressures and in the presence of a catalyst to form mercaptans (*q.v.*):



Other catalysts that have been used for this reaction include metallic sulfides and sulfur. Since mercaptans may add to olefins, sulfides are by-products of the reaction. Passage of an alcohol and hydrogen sulfide over thoria at elevated temperatures also yields the mercaptan:



On reacting with aldehydes or ketones, hydrogen sulfide yields the corresponding thioaldehydes or thioketones. A catalyst is not always necessary for the reaction with aldehydes, but a mineral acid, or zinc chloride, is necessary to promote the reaction with ketones. The thioketones and thioaldehydes have a stronger tendency to polymerize than the parent aldehydes or ketones:



The reactions of polyfunctional carbonyl compounds with hydrogen sulfide are sometimes different from the simple members of the series; for example, thio-phenes have been obtained from 1,4-diketones.

Hexamethylenetetramine reacts with hydrogen sulfide to give the polymer  $(\text{CH}_2\text{S})_x$ .

#### OCCURRENCE

Hydrogen sulfide and other sulfur compounds occur to some extent in most petroleum and natural gas deposits. Particularly large and industrially important quantities are found in the natural gas and petroleum fields of central and north central Wyoming, in western Texas, in southeastern New Mexico, and in Arkansas. Hydrogen sulfide concentrations as high as 42% have been reported (13) in the gas from the Neiber Dome field of central Wyoming. Mineral reserves of hydrogen sulfide in petroleum and natural gas deposits are large. Those in Wyoming are estimated (13) to be about 6,500,000 tons, while by-product hydrogen sulfide produced (but mostly wasted) concurrently with natural gas in western Texas and southeastern New Mexico

is estimated (10) to be over 400 tons per day. Substantial tonnages of hydrogen sulfide are recovered from petroleum refinery operations.

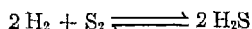
Hydrogen sulfide is occasionally encountered in coal-mining operations. Very substantial quantities of this gas are liberated in coking operations or in the production of manufactured gases from coal. Inasmuch as the hydrogen sulfide is an objectionable impurity in manufactured gas, it is removed, usually by passage through boxes of iron oxide. See *Gas cleaning and purification*. Hydrogen sulfide is present in most volcanic gases, probably having been produced by the action of steam on sulfides at high temperatures. Hydrogen sulfide is also found in numerous "sulfur springs." Its origin in these is at least partly in the bacterial reduction of mineral sulfates. Bacterial reduction of sulfates also accounts for the occurrence of hydrogen sulfide in numerous bodies of water such as the lakes near El Agheila, Libya. Hydrogen sulfide is familiarly formed as a bacterial decomposition product of protein matter, particularly of animal origin.

Hydrogen sulfide is a by-product of many industrial operations. Its production in the natural gas, petroleum, and coal-coking operations has already been mentioned. In general, it is formed whenever sulfur or many sulfur compounds are associated with organic materials at high temperatures. Thus, it is a by-product in the manufacture of carbon disulfide. In the recently developed process in which sulfur reacts with natural gas at elevated temperatures to produce carbon disulfide, half of the sulfur introduced is consumed in the production of hydrogen sulfide. In the older process of reacting sulfur with charcoal, smaller but still important quantities of hydrogen sulfide are produced.

The Disco process for the manufacture of reactive petroleum coke produces as a by-product very large quantities of hydrogen sulfide. The process for producing thiophene by reaction of sulfur with butane at elevated temperatures also produces hydrogen sulfide as a by-product. The refining of sulfur by distillation produces small quantities of hydrogen sulfide. In the coagulation of viscose rayon, some 6 to 9 tons of hydrogen sulfide are formed per 100 tons of rayon produced. Most of this is wasted. Hydrogen sulfide can also be recovered from sulfite waste liquors in the pulp and paper industry.

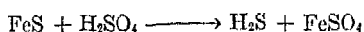
#### PREPARATION AND RECOVERY

Hydrogen sulfide may be prepared by direct synthesis from hydrogen and sulfur vapor:



This reaction proceeds at a satisfactory rate at about 500°C. in the presence of a catalyst such as bauxite or aluminum hydrosilicate minerals. Yields of 96% on a sulfur basis are obtained. Manufacture by this means is economical only if hydrogen is a waste product at the location. The hydrogen sulfide so produced is essentially free of carbon dioxide or other acidic gases and is therefore well suited to the preparation of sodium sulfide and sodium hydrosulfide.

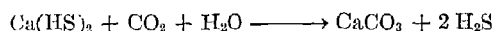
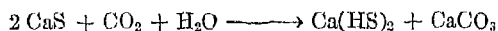
For laboratory purposes, hydrogen sulfide is conveniently prepared by the action of an acid on iron sulfide:



This reaction is usually run in a Kipp generator. The gas so produced contains as impurities traces of hydrogen and arsine. The latter may be removed by passing the

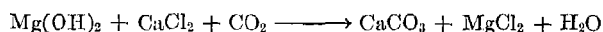
gas over alkali polysulfide at 350°C. In place of iron sulfide, which may contain arsenic or free iron, it has been suggested that manganese sulfide, antimony sulfide, zinc sulfide, or sodium hydrosulfide be used for supplying the sulfur for the laboratory H<sub>2</sub>S generator. Small laboratory quantities of hydrogen sulfide may be conveniently prepared by heating a mixture of sulfur and a hydrogen-rich organic material such as paraffin, naphthalenes, resins, soaps, etc. To facilitate the smooth evolution of gas, asbestos or diatomite is used as a catalyst and suspending agent. Evolution of gas becomes rapid at temperatures from 280 to 320°C.

Primarily of historical interest, the Claus-Chance process recovered large ton-nages of hydrogen sulfide from the waste calcium sulfide of the Leblanc soda process by treatment with carbon dioxide:



Lime kiln gas was first introduced into a slurry of the waste calcium sulfide to form as the net reaction Ca(SH)<sub>2</sub> and calcium carbonate and leave unreacted nitrogen, which was discarded. The Ca(SH)<sub>2</sub> was then further carbonated to calcium carbonate and the exit gases contained relatively high concentrations of hydrogen sulfide. This hydrogen sulfide was converted to sulfur.

Also of historical interest is the Schaffner and Helbig process for recovery of hydrogen sulfide from the same waste calcium sulfide. In this process calcium sulfide slurry was treated at or near the boiling point with a concentrated magnesium chloride solution to yield hydrogen sulfide, calcium chloride, and magnesium hydroxide. The magnesium chloride was recovered by carbonating the slurry of calcium chloride and magnesium hydroxide to yield magnesium chloride and calcium carbonate. The reactions involved were:



**Recovery of By-Product Hydrogen Sulfide.** By far the greatest quantities of hydrogen sulfide produced are obtained as by-products of other operations. Frequently the recovery of the hydrogen sulfide is motivated more by the need to purify the source material than by the value of the recovered gas. (See *Gas cleaning and purification*.) This is particularly true in the petroleum, natural gas, and manufactured gas operations from which the bulk of the hydrogen sulfide is recovered.

Several processes are in use for the recovery of hydrogen sulfide from industrial gases. These are listed in Table IV.

TABLE IV. Principal Processes in Use for the Recovery of Hydrogen Sulfide from Industrial Gases.

Process	Inventor	Company	U.S. patent and year	Absorbent
Girbotol	R. R. Bottoms	The Girdler Corp.	1,783,901 (1930)	Aliphatic amines
Shell phosphate	L. Rosenstein and G. A. Kramer	Shell Development Co.	1,945,163 (1934)	K <sub>2</sub> PO <sub>4</sub>
Alkazid	Hans Baehr	Germany	1,990,217 (1935)	Salts of amino acids
Phenolate	J. A. Shaw	Koppers Co.	2,028,124 (1936)	Sodium phenolate
Vacuum carbonate	A. R. Powell and H. A. Gollmar	Koppers Co.	2,242,323 (1941)	Na <sub>2</sub> CO <sub>3</sub>
			2,379,076 (1945)	
			2,464,805 (1945)	

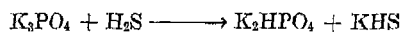


All of these processes employ the same basic flow scheme. The gas containing hydrogen sulfide is introduced into the bottom of a contacting tower or absorber, down through which a solution of the absorbing agent flows. As the gas rises through the tower, its hydrogen sulfide is absorbed, the gas leaving the top of this tower being essentially free of hydrogen sulfide. The hydrogen-sulfide-bearing solution leaving the bottom of the tower is sometimes heated by passage through a heat exchanger before being introduced into the top of a reactivating tower. The solution flows down through the reactivating tower counter to a flow of steam generated at the bottom of the tower by boiling the solution. The rising steam strips the hydrogen sulfide from the absorbent, and upon leaving the reactivating tower is condensed, thereby leaving the hydrogen sulfide available for further use. The stripped solution leaving the bottom of the reactivator is run through a heat exchanger (if one is used) to recover part of the heat of the operation, is further cooled, and is then recycled through the absorber. The absorber and reactivator may be either packed towers or bubble-plate towers.

*The Girbotol process* is the most widely used process for removal of hydrogen sulfide from natural and refinery gases. The absorbent used in this process is usually an aqueous solution of either monoethanolamine or diethanolamine. Triethanolamine, which was used in early installations at a time when it was the only such amine commercially available, has since been largely replaced in the treatment of natural gas by the more reactive monoethanolamine. Diethanolamine, because of its inertness toward carbonyl sulfide, is used largely in the treatment of refinery gases, which often contain this impurity. Monoethanolamine reacts with carbonyl sulfide to form the relatively heat-stable compound diethanolurea,  $\text{CO}(\text{NHCH}_2\text{CH}_2\text{OH})_2$ . See also *Ethanolamines*.

The relatively high cost of the ethanolamines necessitates special precautions to avoid either physical or chemical losses of the absorbent. Thus, the impurities in manufactured gases (primarily tars, cyanogen, and oxygen) have prevented the use of amine solutions in the commercial purification of such gases. A relatively small amount of steam is required to strip the amine solution down to a few grains of hydrogen sulfide per gallon. This complete removal of hydrogen sulfide from the solution permits equally efficient (negative lead acetate test) removal of hydrogen sulfide from the treated gas in the absorbing cycle. These advantages, in large measure, account for the widespread use of the Girbotol process.

*The Shell phosphate process* is essentially similar to the Girbotol process but uses solutions containing over 40% of tripotassium phosphate as the absorbent. The reaction is:



The low volatility of this material permits use of live steam for stripping in place of a reboiler, with some saving in investment. The material is also somewhat more stable chemically, thereby reducing losses from this source. Still another advantage of this process is that some degree of selectivity in the absorption of hydrogen sulfide in the presence of carbon dioxide is obtained. This selectivity is based upon the greater rate of solution of hydrogen sulfide over that of carbon dioxide. Against these advantages is the disadvantage that somewhat more steam is required for reactivation than is required in the Girbotol process.

*The vacuum carbonate process* was developed by Koppers Company as a modifica-

tion of their Seaboard carbonate process (see p. 395) to permit recovery of the hydrogen sulfide. The absorbent in this process is a 3.0 to 3.5% solution of sodium carbonate. The reaction involved is:



In order to reduce the quantity of steam needed for stripping, the reactivation is carried out under a vacuum of about 25 in. Hg. This results in a threefold saving: (1) while the volume of steam used for stripping is the same as would have been used at atmospheric pressure, its weight is only about one-fifth as much; (2) the stripping can be accomplished at about the same temperature (53°C.) as the absorption, thereby reducing the need to transfer sensible heat; and (3) the low pressure of operation permits the use of low pressure exhaust steam for reactivation. The low cost of the absorbent solution and its relative chemical stability permit use of this process in the recovery of hydrogen sulfide from manufactured gases.

The *Alkazid and phenolate processes* are not used in the United States at the present time. The Alkazid process was developed and used in Germany before World War II where some 1,000,000 cu. ft. of  $\text{H}_2\text{S}$  was being removed by the process daily. Three absorbents are used in the process, Alkazid solutions "M," "Dik," and "S." Solution "M" contains sodium alanine and is used for removal of either or both hydrogen sulfide and carbon dioxide. Solution "Dik" contains the potassium salt of dimethylglycine; it is used for the selective removal of hydrogen sulfide in the presence of carbon dioxide. Solution "S" contains sodium phenolate. Operation of the process with solutions "M" or "Dik" presents severe corrosion problems.

The phenolate process was developed by the Koppers Company for removing hydrogen sulfide from manufactured gases. The process employs a solution of sodium phenolate as the absorbent. Operating difficulties encountered in this process have caused the few plants in which this process was operated to be converted to other processes.

*Other Processes.* In addition to the processes described in the previous section, there are a number of others for removing hydrogen sulfide from industrial gases. These, however, do not recover the hydrogen sulfide as such, and in some cases are used as the final "clean-up" operation after one of the preceding operations has removed most of the gas.

Of perhaps greatest economic importance is the "*dry-box*" process for removing hydrogen sulfide from coke-oven gases and other industrial gases. In this process, hydrated iron oxide is coated on shavings or other supporting material spread on trays in rectangular boxes. The gas, to which sufficient air has been added to provide an oxygen concentration of 0.6 to 1.0%, is passed over the iron oxide. The hydrogen sulfide reacts to form ferric sulfide which, in turn, is reoxidized by the added oxygen to the original iron oxide and sulfur. After some use, it is necessary to remove the iron oxide and allow it to become thoroughly revived in the air before returning it to the boxes for further use. The iron oxide is finally discarded when the total sulfur content reaches 50 to 60%. When used for final clean-up, the oxide may be discarded with a sulfur content as low as 30%. Advantages of the dry-box process are the completeness of its removal of hydrogen sulfide and the simplicity of the process. The dry-box process is one of the most selective methods of removing hydrogen sulfide in the presence of carbon dioxide.

A process related to the dry-box process has been used in several plants in Ger-

many. In this process, gas to which the stoichiometric amount of oxygen and 10 to 15 grains of ammonia per 100 cu.ft. have been added is passed over activated carbon. The hydrogen sulfide is thereby converted into sulfur, which can then be recovered by extraction with ammonium sulfide solution. The hydrogen sulfide content of the treated gas is reduced to 0.04 to 0.08 grain per 100 cu.ft.

The *Seaboard process*, developed by Koppers Company in 1920, is similar to the more recently developed vacuum carbonate process (see p. 393). However, instead of employing steam under reduced pressure to reactivate the carbonate solution, large volumes of air are employed to strip the hydrogen sulfide from the absorbent. The hydrogen sulfide is not usually recoverable from this process. The air used in the reactivation operation tends to oxidize some of the hydrogen sulfide to thiosulfate; hence, it is necessary to discard some of the absorbent periodically and add fresh solution to maintain the desired composition (3.0 to 3.5%  $\text{Na}_2\text{CO}_3$ ). Removal of hydrogen sulfide from the treated gas by this process is not usually complete.

Somewhat related to the Seaboard process are the processes that recover the hydrogen sulfide as elementary sulfur. These again absorb the hydrogen sulfide in dilute solutions of sodium carbonate, but, instead of reactivating the solution by desorption of the gas with air, it is oxidized by air in the presence of a catalyst to elementary sulfur. In the *Ferrox process*, a suspension of iron oxide is used as the catalyst, and, in the *nickel process*, nickel sulfate is generally employed. In the *Thylox process*, a neutral solution of sodium thioarsenate is used instead of sodium carbonate, both as the absorbent and as the oxidation catalyst. Because of its larger yield of precipitated sulfur and lower loss of absorbent, the Thylox process has largely replaced the Ferrox and nickel processes.

In these processes, the absorbent is regenerated in tall flooded towers. These vessels are sometimes more than 100 ft. high and, in some plants, two or more may be used in series. Both compressed air and preheated foul solution are introduced into the bottoms of these vessels. The air bubbles up through the solution and oxidizes the hydrogen sulfide. The precipitated sulfur clings to the air bubbles and rises with them to the surface of the solution, where it gathers as a froth. The froth and regenerated solution are separated. The froth is filtered and washed on continuous filters to yield a product containing about 50% finely divided sulfur and 50% water plus small quantities of impurities. These impurities, unless removed by further refining of the sulfur, limit the usefulness of the product to agricultural fungicides and other less critical uses.

About 10 to 15% of the absorbed hydrogen sulfide is oxidized to thiosulfate in the Thylox process, while 30 to 40% is so oxidized in the Ferrox or nickel processes. It is necessary, therefore, to replace part of the solution continuously to maintain the desired composition of the absorbent. Another disadvantage of the process is the relatively poor removal of hydrogen sulfide from the treated gas, 90-95% removal being usual.

Where complete removal of relatively small quantities of hydrogen sulfide is necessary, it is the practice to use sodium hydroxide solutions. This is normally a batch operation, the solution being replaced when most of the sodium hydroxide has been converted into sodium sulfide. Gas-liquid contacting devices employed to effect this reaction include packed towers, and jet scrubbing devices, and simply bubbling the gas through the solutions. In some cases the removal of hydrogen sulfide is carried out in two stages, the gas being first contacted with a solution of sodium sulfide,

which is converted to the hydrosulfide, concentrated, and sold. The gas is then contacted with a solution of sodium hydroxide, which completely removes the remaining traces of hydrogen sulfide from the gas, the solution being converted to sodium sulfide, which is later converted to sodium hydrosulfide.

Calcium hydroxide is a less expensive base, but its insolubility and that of calcium sulfide cause process difficulties. It is, therefore, less frequently used than sodium hydroxide.

Where hydrogen sulfide must be removed from acid gases such as carbon dioxide, alkaline absorbents cannot be used. In these cases, oxidizing agents such as potassium permanganate solution or a buffered solution of sodium dichromate and zinc sulfate may be used. These reagents are relatively expensive and hence may be economically employed only where the concentration of hydrogen sulfide is small.

The addition of chlorine has been used to remove hydrogen sulfide from the vent gases of viscose rayon factories. Less than stoichiometric quantities of chlorine are required for complete removal of hydrogen sulfides, the chlorine apparently serving also as a catalyst for the atmospheric oxidation of the hydrogen sulfide. This method, however, presents severe corrosion problems (19).

#### ECONOMIC ASPECTS OF BY-PRODUCT HYDROGEN SULFIDE RECOVERY

Recovery of by-product hydrogen sulfide has increased rapidly since World War II, the total being over 217,000 tons in 1950; over 550,000 tons are anticipated for 1953. Several factors have stimulated this increase in the recovery of hydrogen sulfide. Advancing prices of sulfur since World War II have increased the number of recovery operations which are economically feasible. The need to process petroleum crudes and natural gases of higher sulfur contents has increased the quantities of hydrogen sulfide available for recovery. Also, the need to reduce atmospheric pollution has added further stimulus to the recovery of hydrogen sulfide.

Table V gives statistics on the recovery of hydrogen sulfide (reported as long tons of elementary sulfur). (U.S. Bureau of Mines *Minerals Yearbook* 1950.)

TABLE V. Recovery of By-Product Hydrogen Sulfide.

Year	Long tons of elemental sulfur from by-product $H_2S$	Long tons of sulfur contained in $H_2SO_4$ from by-product $H_2S$
1939	4,307	13,000
1947	43,427	20,631
1948	44,369	25,792
1949	56,781	37,935
1950	142,475	39,889

The value of recovered hydrogen sulfide depends upon the quantity available, its location, and the use to which it is to be put, that is, whether it is to be converted into elemental sulfur or sulfuric acid. If the hydrogen sulfide is to be converted to sulfuric acid, its value is very nearly that of the sulfur which it contains. However, if it is to be converted to elemental sulfur, the cost of conversion (about \$6 or \$7 per ton for a 50-ton-per-day plant) must be taken into consideration. At least one sulfur recovery plant has paid a royalty of 3/16 of the market value of the sulfur produced from hydrogen sulfide.

## MATERIALS OF CONSTRUCTION

Anhydrous hydrogen sulfide is relatively noncorrosive to carbon steel and a wide variety of metals and alloys including aluminum, Stellite, Inconel, Ni-Resist, and types 304 and 316 stainless steels. However, all hard magnetic steels if highly stressed are subject to hydrogen embrittlement by hydrogen sulfide, the hydrogen possibly resulting from slight corrosion of the metal by the hydrogen sulfide. This can be prevented by coating the steel with aluminum or Teflon or by replacing the steel with an alloy such as age-hardened Inconel or type 316 stainless steel (3).

In the presence of moisture, hydrogen sulfide is much more corrosive, carbon steel being corroded at rates in the vicinity of 0.1 in. per year. The rate of corrosion is a function of local conditions and other materials present. The stainless steels (particularly type 316) will often be found satisfactory. In a Girbotol process absorbing gas having a 5 to 1 ratio of carbon dioxide to hydrogen sulfide and using as an absorbent monoethanolamine (15%), diethylene glycol (80%), and water (5%), steels containing either 2.5% chromium and 1% molybdenum or 4-6% chromium and 0.5% molybdenum showed no corrosion. The 2-S or 3-S aluminum alloys and 18-8 chrome-nickel stainless steels were also satisfactory.

## HEALTH AND SAFETY FACTORS

Hydrogen sulfide is one of the more dangerous materials of industry. In its handling, two types of hazards must be taken into account, its extreme toxicity and its explosive nature when mixed with air or sulfur dioxide.

Of perhaps greatest importance is its extreme toxicity. Its maximum safe concentration is about 13 p.p.m. While this concentration can at first be readily recognized by its odor, hydrogen sulfide may partially paralyze the olfactory nerves to the point at which the presence of the gas is no longer sensed. Hence, the odor of the gas is not a reliable safeguard or warning against its poisonous effects. Hydrogen sulfide, in its toxic action, attacks the nerve centers. Early symptoms of poisoning are slight headache, burning eyes, and clouded vision.

Some precautions against poisoning to be followed in working with hydrogen sulfide are:

1. Closed-in areas should be well ventilated, preferably with a forced draft.
2. Equipment containing hydrogen sulfide should be maintained tight. Any leaks should be repaired immediately.
3. At seals or stuffing boxes where leaks might occur during normal operation, means should be provided for venting the escaped gas to a safe location.
4. Vessels should be purged of hydrogen sulfide before being opened.
5. Masks furnishing pure air should be worn by personnel who are likely to be exposed to the gas.
6. Personnel who may be exposed to low concentrations of the gas should frequently retire to areas of fresh air.
7. As a good safety measure, personnel should learn to recognize the early symptoms of hydrogen sulfide poisoning.

Hydrogen sulfide is a combustible material, and, when in mixture with air or sulfur dioxide may be explosive. It is essential, therefore, to avoid such mixtures in the processing of hydrogen sulfide. The explosive range of hydrogen sulfide in air is from 4.5 to 45.5%. The ignition temperature of such mixtures is around 250°C.

## USES

The great bulk of the hydrogen sulfide, recovered as a by-product, is converted either into elementary sulfur or into sulfuric acid. When there is a market for sulfuric acid in the vicinity of the source of hydrogen sulfide, it is economical to convert the hydrogen sulfide directly to sulfuric acid without going through the intermediate sulfur step. However, when there is insufficient market for the acid near the source of recovered hydrogen sulfide, it is usually converted into elementary sulfur.

Conversion of hydrogen sulfide into sulfur is advantageous because sulfur is a stable, easily stored, easily shipped product for which there is a very broad market. The bulk of the hydrogen sulfide is converted into sulfur by modifications of the Claus process (see *Sulfur*). Smaller quantities are converted into sulfur paste by the Thylox process (see p. 395). Because of the large quantities involved, hydrogen sulfide has become an important source of elementary sulfur.

Hydrogen sulfide finds use in the preparation of various sulfides. Considerable quantities of hydrogen sulfide are used in the manufacture of sodium sulfide and sodium hydrosulfide.

Hydrogen sulfide is used in the preparation of organic sulfur compounds such as the thiophenes, mercaptans, sulfides, etc. Sulfur-containing additives for extreme-pressure lubricants and cutting oils are prepared by reaction of hydrogen sulfide with various organic reagents. Tertiary olefins, for example, are reacted at high pressure and temperature with liquid hydrogen sulfide to form tertiary alkyl mercaptans.

Hydrogen sulfide is sometimes used to remove arsenic from 53°Bé. chamber process sulfuric acid (*q.v.*) produced from pyrites. Inasmuch as this treatment also removes other heavy metallic impurities, acid treated in this manner is relatively pure.

Hydrogen sulfide is a familiar reagent in the chemical laboratory, where it is used as a precipitating agent in the usual scheme of qualitative analysis.

## Hydrogen Polysulfides

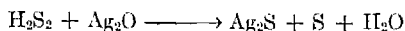
**Hydrogen polysulfides** (hydrogen persulfides),  $H_2S_x$ , are yellow, oily liquids formed when alkali or alkaline earth polysulfide solutions are added to mineral acid solutions. They were first observed in 1777 by Scheele, who noted that a yellow, pungent, oily substance resulted from the rapid addition of much acid to a solution of sulfur in an alkali.

The hydrogen polysulfide formed upon addition of an alkali polysulfide solution to acid is generally a mixture of compounds, the following of which have been isolated and characterized:  $H_2S_2$ ,  $H_2S_3$ ,  $H_2S_4$ ,  $H_2S_5$ , and  $H_2S_6$ , and probably a continuous series.

The polysulfides of hydrogen may be separated by fractional distillation. The higher polysulfides are particularly subject to thermal decomposition, hence an extremely high vacuum is required in their distillation. The separation of  $H_2S_5$  and  $H_2S_6$  is accomplished at  $10^{-4}$  mm. Hg. The decomposition of  $H_2S_x$  results in hydrogen sulfide and sulfur.

**Hydrogen disulfide** (hydrogen persulfide),  $H_2S_2$ , formula weight 66.15, is an unstable yellow flammable liquid with a pungent odor whose vapors attack the eyes and mucous membranes. M.p.  $-89.6^\circ\text{C}.$ ; b.p.  $70.7^\circ\text{C}.$ ;  $d_4^{20}$  1.3339; heat of fusion 27.2 cal./gram; heat of vaporization 129.2 cal./gram;  $C_p$  0.334 cal./gram; surface tension 38.1 dynes/cm. It is miscible with carbon disulfide, benzene, and ether. It is a good solvent for sulfur.

Hydrogen disulfide is extremely sensitive to alkalis, and it is necessary to treat the glass or silica vessel in which it is kept with HCl to prevent decomposition. Correspondingly, it is rapidly decomposed by water and by alcohols, and almost explosively if the water is alkaline. It is oxidized by silver oxide:



It is also oxidized by concentrated sulfuric acid to sulfur dioxide. Hydrogen disulfide forms addition compounds with aldehydes and ketones.

Hydrogen disulfide may be prepared by the thermal decomposition of crude hydrogen polysulfide or of hydrogen trisulfide at temperatures ranging from 100 to 150°C. and at reduced pressures. Best yields are obtained from a crude prepared from  $\text{Na}_2\text{S}_{2.5}$ . The product is purified by fractional distillation.

**Hydrogen trisulfide**,  $\text{H}_2\text{S}_3$ , formula weight 98.21, is an unstable, pale yellow, mobile oil with a disagreeable pungent odor suggesting camphor and sulfur chloride. M.p.  $-52^\circ\text{C}.$ ; b.p.  $69^\circ\text{C}.$  at 2 mm.; sp. gr. 1.496. It is slightly less sensitive to the presence of alkalis than is hydrogen disulfide but is more easily decomposed by elevated temperatures. It is soluble in carbon disulfide, benzene, chloroform, ether, and similar solvents, and is itself a solvent for sulfur. It is decomposed by water, alkalis, and alcohols. It forms very unstable addition products with ketones and aldehydes. When distilled at atmospheric pressure, it decomposes, about one-third being converted into hydrogen disulfide. Exposure to light accelerates its decomposition. It slowly reduces concentrated sulfuric acid. It is oxidized by dry silver oxide, cupric oxide, lead dioxide, and mercuric oxide, the metallic sulfides being thereby obtained. Its oxidation by potassium permanganate or dichromate is violent.

**Hydrogen tetrasulfide**,  $\text{H}_2\text{S}_4$ , **hydrogen pentasulfide**,  $\text{H}_2\text{S}_5$ , and **hydrogen hexasulfide**,  $\text{H}_2\text{S}_6$ , are yellow, oily liquids obtained by fractional distillation of crude hydrogen polysulfide at  $10^{-4}$  mm. Hg. They have no definite melting points.

Compound	Formula wt.	$d_4^{15}$
$\text{H}_2\text{S}_3$	130.28	1.588
$\text{H}_2\text{S}_5$	162.35	1.660
$\text{H}_2\text{S}_6$	194.41	1.699

These compounds are very unstable. They are decomposed on contact with powdered quartz and glass, wood, or paper. They are soluble in benzene and similar solvents, and are themselves solvents for sulfur (17).

A crude hydrogen pentasulfide is obtained by treating pure dry ammonium pentasulfide crystals with carefully dried formic acid. The molecular weight of the product so produced is 152.5, as determined by cryoscopic measurement in benzene.

### Sulfur Halides and Oxyhalides.

Sulfur combines with halogens to form several series of halides. The compounds so formed generally become less stable as the atomic weights of the halogens increase. This is particularly true for the compounds containing large atomic fractions of halogen. Thus sulfur hexafluoride is an extremely inactive gas, while no compounds of sulfur and iodine have ever been isolated. The known halides of sulfur are listed in Table VI. For oxyhalides see p. 405.

TABLE VI. Halides of Sulfur.

Fluorides (see Vol. 6, p. 732) . .	SF <sub>6</sub>	S <sub>2</sub> F <sub>10</sub>	SF <sub>4</sub> (uncertain)	SF <sub>2</sub>	S <sub>2</sub> F <sub>2</sub>
Chlorides . . . . .	—	—	SCl <sub>4</sub>	SCl <sub>2</sub>	S <sub>2</sub> Cl <sub>2</sub>
Bromides . . . . .	—	—	—	—	S <sub>2</sub> Br <sub>2</sub>
Iodides . . . . .	None isolated				

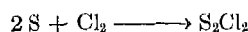
### Sulfur Monobromide.

Sulfur monobromide (disulfur dibromide), S<sub>2</sub>Br<sub>2</sub>, formula weight 223.96, is the only definite bromide of sulfur. It is a garnet-red, oily liquid, m.p.  $-46^{\circ}\text{C}.$ ; b.p.  $54^{\circ}\text{C}.$  at 0.18 mm.;  $d_4^{20}$  2.6355. It is prepared by the reaction of an equiatomic mixture of sulfur and bromine, preferably at  $100^{\circ}\text{C}.$ , in a sealed vessel. Sulfur monobromide is soluble in carbon disulfide and similar solvents, and is a solvent for sulfur. It is chemically similar to sulfur monochloride, but is less stable.

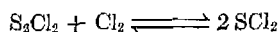
### Sulfur Chlorides.

Chlorine and sulfur react readily to form a series of compounds including the following well established members: SCl<sub>4</sub>, SCl<sub>2</sub>, and S<sub>2</sub>Cl<sub>2</sub> as well as S<sub>3</sub>Cl<sub>2</sub>, S<sub>4</sub>Cl<sub>2</sub>, . . . , S<sub>2</sub>Cl<sub>8</sub>, and S<sub>8</sub>Cl<sub>4</sub>, whose existences are somewhat less certain.

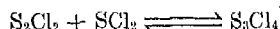
The initial reaction between sulfur and chlorine yields sulfur monochloride S<sub>2</sub>Cl<sub>2</sub>:



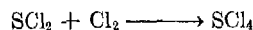
Upon further addition of chlorine sulfur dichloride, SCl<sub>2</sub>, is slowly formed:



At low temperatures, S<sub>2</sub>Cl<sub>2</sub> and SCl<sub>2</sub> combine to form trisulfur tetrachloride, S<sub>3</sub>Cl<sub>4</sub>. This compound is, however, largely decomposed at room temperature:



When chlorine is added to sulfur monochloride or sulfur dichloride at low temperatures, sulfur tetrachloride is formed:



Freezing points of the chlorine-sulfur system lying between S<sub>2</sub>Cl<sub>2</sub> and sulfur suggest the existence of S<sub>3</sub>Cl<sub>2</sub> and S<sub>4</sub>Cl<sub>2</sub>. It is probable that "chlorine polysulfides" containing even longer chains of sulfur have at least transient existence.

### Sulfur Monochloride.

Sulfur monochloride (disulfur dichloride), S<sub>2</sub>Cl<sub>2</sub>, formula weight 135.04 is a golden-yellow liquid, with a pungent odor, which was first studied in 1810 by Davy and Buchholz. It is most readily formed by the direct combination of chlorine and sulfur, but may be obtained by a wide variety of other reactions including the action of chlorine on numerous sulfides or the action of higher-valence chlorides such as phosphorus pentachloride or mercuric chloride on sulfur.

M.p.  $-82^{\circ}\text{C}.$ ; b.p.  $138^{\circ}\text{C}.$ ; sp.gr.,  $d_4^{25}$  1.6733; heat of vaporization 64.6 cal./gram;  $C_p$  (liquid) 0.220 cal./g.; heat of formation  $-106$  cal./gram (liquid at  $18^{\circ}\text{C}.$ );

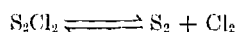


surface tension at 22°C. 40.78 dynes/cm.; viscosity at 18°C. 2.015 cps. The vapor pressure of sulfur monochloride is given in mm. by the equation:

$$\log p = 7.4550 - 1880.1/T \quad (T = ^\circ\text{K.})$$

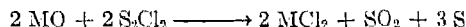
The boiling point elevation constant is 52.9.

Sulfur monochloride is quite stable at room temperature; but experiments with radioactive sulfur in solution in sulfur monochloride at 100°C. demonstrate an appreciable rate of exchange of sulfur between the two materials. This indicates a reversible breakdown of the sulfur monochloride at 100°C. The breakdown does not, however, become important until temperatures in excess of 300°C. are reached. At this temperature the decomposition is:

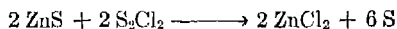


Sulfur chloride is noncombustible at room temperature; but at elevated temperatures decomposition is sufficiently rapid to permit the liberated sulfur to burn, producing sulfur dioxide, sulfur trioxide and chlorine.

Many metallic oxides are attacked by sulfur monochloride, yielding the corresponding chlorides:



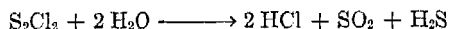
Metallic sulfides react similarly:



Sulfur trioxide reacts with sulfur monochloride to give pyrosulfuryl chloride,  $\text{S}_2\text{O}_6\text{Cl}_2$ . Sulfates heated with sulfur monochloride are converted to chlorides, sulfuryl chloride being simultaneously formed:



Sulfur monochloride is hydrolyzed with water, slowly at room temperature but rapidly at elevated temperatures. The rate of hydrolysis in the vapor state is rather slow:

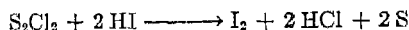


In solution, the hydrogen sulfide and sulfur dioxide react further to produce sulfur and polythionic acids. In the presence of additional chlorine, the hydrolysis produces sulfuric acid:

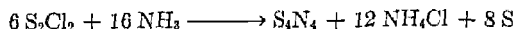


This reaction may occasionally be useful in dehydrations.

With iodides, sulfur monochloride liberates iodine, a reaction useful in its analysis:

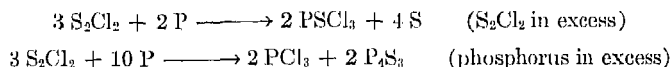


When treated with dry ammonia in a suitable solvent, at low temperatures, it yields sulfur nitrides:

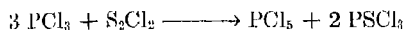


When an excess of  $\text{S}_2\text{Cl}_2$  is treated with phosphorus, phosphorus sulfochloride,

$\text{PSCl}_3$ , and free sulfur are formed. However, when phosphorus is in excess, then phosphorus trichloride and phosphorus sulfide are formed:

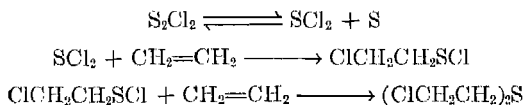


In the presence of iodine as a catalyst, sulfur monochloride reacts with phosphorus trichloride to produce phosphorus pentachloride and phosphorus sulfochloride:



Antimony pentachloride, boron trichloride, and ferric chloride react with sulfur monochloride and chlorine to form complexes,  $\text{SbCl}_5 \cdot \text{S}_2\text{Cl}_2$ ,  $\text{BCl}_3 \cdot \text{S}_2\text{Cl}_2$ , and  $\text{FeCl}_3 \cdot 2\text{S}_2\text{Cl}_2$ . The iron complex reacts with organic acids to form the corresponding acyl chlorides.

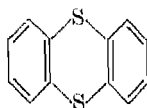
With organic reagents, sulfur monochloride reacts to introduce either or both sulfur and chlorine. Thus, in its well-known reaction with ethylene to produce mustard gas (see *Gas warfare agents*), both sulfur and chlorine are introduced. The reaction is believed to proceed in steps as follows:



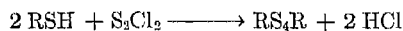
When sulfur monochloride is reacted with aromatic hydrocarbons, the corresponding aromatic dithiochlorides are formed:



These compounds in turn react with additional hydrocarbon to produce a variety of sulfides. Thus, the reaction of sulfur monochloride with benzene in the presence of zinc yields  $\text{C}_6\text{H}_5\text{SC}_6\text{H}_5$ ,  $\text{C}_6\text{H}_5\text{SH}$ ,  $\text{C}_6\text{H}_5\text{SSC}_6\text{H}_5$ , and thianthrene:



When reacted with mercaptans sulfur monochloride yields tetrasulfides:



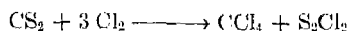
Because of its dehydrating action, sulfur chloride reacts with organic acids to form the corresponding acid anhydrides. With the higher aliphatic acids, the acid chlorides are produced.

#### MANUFACTURE

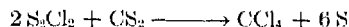
The sulfur monochloride of commerce is usually produced by direct combination of the elements in batch processes carried out in horizontal steel vessels. The process consists of charging refined sulfur to a reactor that contains sufficient sulfur chloride from a previous batch to cover the sparger through which the chlorine is to be introduced. The batch is heated to 50–60°C. to facilitate the initiation of the reaction, and chlorine is then metered into the batch until the desired degree of chlorination has been obtained. Since the reaction is exothermic and not very rapid, the rate of chlorine addition must be controlled to prevent excessive loss of this reactant or of sulfur dichloride that may be formed as an intermediate compound.

The chlorination of sulfur is a progressive reaction that no doubt starts with the chlorination of the free ends of ruptured  $S_8$  rings. The  $S_8Cl_2$  thus formed is unstable and breaks down into smaller fragments, which either reorient themselves to shorter chain chlorides or in turn become further chlorinated, ultimately to  $SCl_2$ . The compound  $S_2Cl_2$  appears to be the most stable member of the series; the stability of the individuals falling off as the length of the sulfur chain increases (or decreases). Since the reactions in this series are relatively slow, equilibrium among the various products may not be maintained during the chlorination if this operation is carried on rapidly; both  $SCl_2$  and higher sulfur chlorides are present when the average composition reaches that of  $S_2Cl_2$ . Commercial batches are produced sufficiently slowly to yield a product which is largely  $S_2Cl_2$  at the end of the chlorination.

Large quantities of sulfur monochloride appear as an intermediate product in the manufacture of carbon tetrachloride from carbon disulfide and chlorine:



The mixture of carbon tetrachloride and sulfur monochloride is separated by fractional distillation to yield a concentrated sulfur monochloride, which is, however, too impure to be marketed as a commercial grade. It contains carbon tetrachloride, sulfur, tars, traces of carbon disulfide, etc. The crude sulfur monochloride is treated with additional carbon disulfide in the presence of a catalyst to yield more carbon tetrachloride and sulfur:



Sulfur monochloride vapor is extremely toxic, the threshold limit of toxicity being about 1 p.p.m. It is very irritating to the eyes and mucous membranes. The liquid is also extremely corrosive to the skin. It is necessary, therefore, to follow the usual precautions for handling toxic and corrosive volatile liquids.

Dry sulfur monochloride is not corrosive to iron or steel at ordinary temperatures, but is very corrosive in the presence of moisture, and it is essential to exclude moisture from any equipment in which it is stored.

Commercial sulfur monochloride is produced in a variety of grades depending upon the ratio of sulfur to chlorine. "Yellow sulfur chloride" may contain from 0 to 7% excess sulfur; "red sulfur chloride" is usually a mixture of sulfur mono- and dichlorides in varying proportion. Sulfur monochloride is shipped in 7000 to 8000 gal. tank cars containing about 100,000 lb.; in 55 gal. steel drums containing 700 lb., or in 10 gal. drums containing 130 lb. It is shipped as a corrosive liquid under a White label. The price in tank car lots in March 1954 was 4 cents per pound.

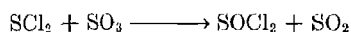
#### USES OF SULFUR CHLORIDES

Sulfur monochloride in combination with chlorine is often used as a substitute for sulfur dichloride. Hence, the uses considered here will include those for sulfur dichloride.

Sulfur chlorides are useful as chlorinating agents or for introducing sulfur into organic compounds, or both. For example, sulfur monochloride is treated with ethylene to produce mustard gas. Of more importance commercially, considerable sulfur chloride is used in the treatment of unsaturated fatty acids to produce compounds containing chlorine and sulfur. These materials are useful as additives to cutting oils and extreme pressure lubricants. In addition to fatty acids, phenols and a variety

of unsaturated compounds (primarily of petroleum origin) have been treated with sulfur chlorides for the same purpose. Treatments of various vegetable oils such as corn oil, cottonseed oil, rapeseed oil, and soybean oil with sulfur chloride yield rubber-like products, known as factice. The largest outlet for this type of product is in the production of art-gum erasers.

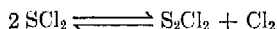
Sulfur dichloride is sometimes used in the treatment of drying oils for varnishes. This use somewhat parallels its use as a drying agent for coatings of ink, paint, or varnish. Sulfur monochloride is used to cold-vulcanize articles made of thin rubber sheets. Toy balloons and drug sundries are examples of such products. Sulfur dichloride or the combination of sulfur monochloride and added chlorine when treated with the sodium salts of organic acids produce the corresponding acid anhydrides. Thus, acetic anhydride is obtained from the action of sulfur chloride on sodium acetate. With the higher aliphatic acid salts, the acid chlorides are produced by this process. Sulfur chlorides are often used as catalysts in the chlorination of organic compounds. Thus sulfur monochloride is used as a catalyst in the chlorination of acetic acid to monochloroacetic acid. The hydrolysis of sulfur monochloride can be made to yield that form of sulfur which is insoluble in carbon disulfide (39). Some uses for sulfur monochloride depend upon its ability to dissolve sulfur. Sulfur dichloride or sulfur monochloride and chlorine are treated with sulfur trioxide to produce thionyl chloride:



### Sulfur Dichloride.

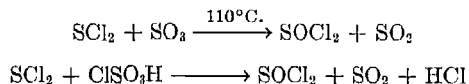
Sulfur dichloride,  $\text{SCl}_2$ , formula weight 102.98, is a dark brown or reddish liquid m.p.  $-122^\circ\text{C}.$ ; b.p. about  $59^\circ\text{C}.$  (some decompn.);  $d_4^{16}$  1.621; vapor pressure at  $-23^\circ\text{C}.$  7.6 mm.; heat of formation at  $25^\circ\text{C}.$   $-116.5$  cal./gram; heat of vaporization at  $59^\circ\text{C}.$  67.6 cal./gram. It decomposes rapidly at temperatures over  $40^\circ\text{C}.$

Chemically, sulfur dichloride behaves very much like a mixture of  $\text{S}_2\text{Cl}_2$  and chlorine. This follows in part, at least, from the equilibrium:

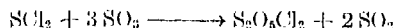


the constant for which is 0.013 at  $18^\circ\text{C}.$

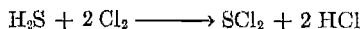
Sulfur dichloride reacts with sulfur trioxide or with chlorosulfonic acid to produce thionyl chloride and sulfur dioxide:



Treatment of sulfur dichloride with an excess of sulfur trioxide yields pyrosulfuryl chloride,  $\text{S}_2\text{O}_5\text{Cl}_2$ :



Sulfur dichloride is the primary product in the gaseous reaction between hydrogen sulfide and chlorine:



However, it is prepared commercially by the addition of chlorine to sulfur monochloride. The reaction proceeds rather slowly, and particularly at its later stages is limited to temperatures below  $40^\circ\text{C}.$  It is carried out in the same equipment used to

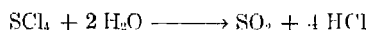
produce the monochloride. The commercial product often contains a small percentage of dissolved free chlorine.

The uses of sulfur dichloride have been discussed with those of the monochloride. Handling precautions and packaging are also similar to those for the monochloride. The price of sulfur dichloride as of March 1954 was 3½ cents per pound in tank car lots.

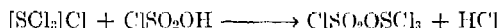
### Sulfur Tetrachloride.

Sulfur tetrachloride (trichlorosulfonium chloride),  $\text{SCl}_4$ , formula weight 173.89, is a yellow solid that melts to a red liquid at about  $-30^\circ\text{C}$ . Even at its melting point, the liquid dissociates into chlorine and sulfur dichloride. It is formed by the addition of chlorine to sulfur dichloride at high pressures and low temperatures. The solid is believed to be the salt,  $[\text{SCl}_3]^+\text{Cl}^-$ .

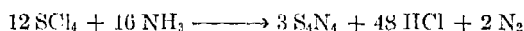
Sulfur tetrachloride reacts rapidly with water to form sulfur dioxide and hydrochloric acid:



It reacts with chlorosulfonic acid to yield a salt (see p. 414):



It reacts with anhydrous ammonia to form sulfur nitride:



Sulfur tetrachloride forms unstable crystalline addition compounds:  $\text{SbCl}_5 \cdot \text{SCl}_4$ , m.p.  $125^\circ\text{C}$ .;  $\text{TiCl}_4 \cdot \text{SCl}_4$ , soluble in carbon disulfide and hydrocarbon solvents;  $\text{SnCl}_4 \cdot 2\text{SCl}_4$ ;  $\text{FeCl}_3 \cdot \text{SCl}_4$ , useful in some chlorination reactions;  $\text{AlCl}_3 \cdot \text{SCl}_4$ ;  $2\text{ICl}_3 \cdot \text{SCl}_4$ , soluble in  $\text{CHCl}_3$ ,  $\text{CCl}_4$ , and hydrocarbon solvents;  $2\text{AsF}_3 \cdot \text{SCl}_4$ ; and  $\text{BCl}_3 \cdot \text{SCl}_4$ , m.p.  $-23^\circ\text{C}$ .

### Oxyhalides

The sulfur oxyhalides may be considered to be the halo derivatives of the sulfur oxygen acids (oxyacids). The known oxyhalides falling into this category are listed below. Though sulfur dichloride and difluoride are not oxyhalides, they are included in Table VII as derivatives of an oxygen acid.

Sulfur oxytetrachloride,  $\text{S}_2\text{O}_3\text{Cl}_4$ , does not fall into the above classification (see p. 414).

### Thionyl Bromide.

Thionyl bromide,  $\text{SOBr}_2$ , formula weight 207.90, is an orange-yellow liquid, sp.gr.,  $d_4^{15}$  2.697, b.p.  $138^\circ\text{C}$ . (with decompn.); vapor pressure, at  $45^\circ\text{C}$ ., 22 mm.; at  $68^\circ\text{C}$ ., 40 mm. It is prepared by the action of  $\text{HBr}$  on  $\text{SOCl}_2$  at low temperatures. Its reactions are similar to those of thionyl chloride but it is less stable, decomposing slowly at room temperature:



It is readily hydrolyzed by water, and reacts with organic acids to form acid bromides.

TABLE VII. Halogen Derivatives of Sulfur Oxygen Acids.

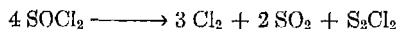
Halogen derivative	Oxygen acid			
	Sulfoxylic HOSOH	Sulfurous	Sulfuric	Pyrosulfuric
		$\begin{array}{c} \text{O} \\ \uparrow \\ \text{HOSOH} \end{array}$	$\begin{array}{c} \text{O} \\ \uparrow \\ \text{HOSOH} \\ \downarrow \\ \text{O} \end{array}$	$\begin{array}{cc} \text{O} & \text{O} \\ \uparrow & \uparrow \\ \text{HO}-\text{S}-\text{O}-\text{S}-\text{OH} \\ \downarrow & \downarrow \\ \text{O} & \text{O} \end{array}$
Oxyfluoride	Sulfur difluoride $\text{SF}_2$	Thionyl fluoride $\text{SOF}_2$	Fluorosulfonic acid $\text{FSO}_3\text{H}$ Sulfuryl fluoride $\text{SO}_2\text{F}_2$	---
Oxychloro- fluoride	---	---	Sulfuryl chlorofluoride $\text{SO}_2\text{FCl}$	---
Oxychloride	Sulfur dichloride $\text{SCl}_2$	Thionyl chloride $\text{SOCl}_2$	Chlorosulfonic acid $\text{ClSO}_3\text{H}$ Sulfuryl chloride $\text{SO}_2\text{Cl}_2$	Pyrosulfuryl chloride $\text{S}_2\text{O}_5\text{Cl}_2$
Oxybromide	---	Thionyl bromide $\text{SOBr}_2$	---	---

### Thionyl Chloride.

Thionyl chloride (sulfurous oxychloride),  $\text{SOCl}_2$ , formula weight 118.98, is a colorless, fuming liquid which finds its primary use as a chlorinating agent in organic chemistry. M.p.  $-104.5^\circ\text{C}$ .; b.p.  $79^\circ\text{C}$ .;  $d_4^{20}$  1.676;  $n_D^{20}$  1.517;  $C_p$  0.24 cal./gram; latent heat of vaporization 62.9 cal./gram; heat of formation  $-47,200$  cal./gram-mole; coefficient of cubical expansion  $0.0010/^\circ\text{C}$ .; viscosity at  $0^\circ\text{C}$ . 0.801 cps., at  $38^\circ\text{C}$ . 0.545 cps.; dielectric constant at  $20^\circ\text{C}$ . 9.25; electrical conductivity at  $25^\circ\text{C}$ .  $2 \times 10^{-6}$  (mho)(cm.)/(sq.cm.). The vapor pressure of thionyl chloride at various temperatures is:

Temperature, $^\circ\text{C}$ .....	20	30	40	50	60	70	75
Vapor pressure, mm. Hg.....	96.6	147.9	221.3	321.6	458.1	637.9	746.0

Thionyl chloride is miscible with benzene, chloroform, carbon tetrachloride, etc. It will dissolve the iodides of arsenic antimony, tin, mercury, cobalt, and tetramethylammonium to give slightly conducting solutions. It forms the addition product  $2\text{AlCl}_3.\text{SOCl}_2$ . Thionyl chloride may be considered to be the chloro derivative of sulfurous acid. It is characterized by its very strong tendency to replace OH or SH groups with chlorine atoms. It will also, under some circumstances, replace  $\text{SO}_2$ , H, or O with chlorine. Thionyl chloride begins to decompose at about  $150^\circ\text{C}$ ., decomposition being largely complete at about  $500^\circ\text{C}$ .:



The ease of decomposition of thionyl chloride accounts for many of its reactions, particularly those at elevated temperatures.

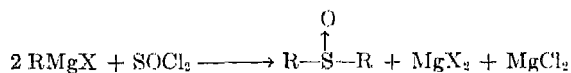
Table VIII summarizes the inorganic reactions of thionyl chloride.

TABLE VIII. Summary of Inorganic Reactions of Thionyl Chloride.

Reactant	Conditions of reaction	Primary reaction products
<i>Reactions characteristic of the thermal decomposition of thionyl chloride</i>		
Sulfur	180°C.	S <sub>2</sub> Cl <sub>2</sub> , SO <sub>2</sub>
Phosphorus	Elevated temp.	PCl <sub>3</sub> , SO <sub>2</sub> , S <sub>2</sub> Cl <sub>2</sub>
Phosphorus	Prolonged heating with excess SOCl <sub>2</sub>	PCl <sub>3</sub> , SO <sub>2</sub> , S <sub>2</sub> Cl <sub>2</sub>
PCl <sub>3</sub>	High temp.	PCl <sub>5</sub> , PSCl <sub>3</sub> , POCl <sub>3</sub>
Selenium	High temp.	SeCl <sub>4</sub> , SO <sub>2</sub> , S
SeO <sub>2</sub>	—	SeCl <sub>4</sub> , SO <sub>2</sub>
Tellurium	SOCl <sub>2</sub> in excess	TeCl <sub>4</sub> , SO <sub>2</sub> , S
Tellurium	Tellurium in excess	TeCl <sub>2</sub> , SO <sub>2</sub> , S
Many metals	Elevated temp.	Metal chlorides, S <sub>2</sub> Cl <sub>2</sub> , SO <sub>2</sub>
Metal sulfides	150–200°C.	Metal chlorides, SO <sub>2</sub> , S <sub>2</sub> Cl <sub>2</sub>
Metal oxides	200°C.	Metal chlorides, SO <sub>2</sub>
<i>Reactions characteristic of thionyl chloride itself</i>		
Water	Low temp., rapid reaction	H <sub>2</sub> SO <sub>3</sub> , HCl
BaO <sub>2</sub>	SOCl <sub>2</sub> in excess	BaCl <sub>2</sub> , SO <sub>2</sub> , SO <sub>2</sub> Cl <sub>2</sub>
BaO <sub>2</sub>	BaO <sub>2</sub> in excess	BaCl <sub>2</sub> , BaSO <sub>4</sub> , SO <sub>2</sub> Cl <sub>2</sub>
Hg or HgO	150°C., excess SOCl <sub>2</sub>	HgCl <sub>2</sub> , SO <sub>2</sub> Cl <sub>2</sub> , S <sub>2</sub> Cl <sub>2</sub>
Hg	150°C., excess Hg	HgCl <sub>2</sub> , SO <sub>2</sub> , S <sub>2</sub> Cl <sub>2</sub>
H <sub>2</sub> S	AlCl <sub>3</sub> catalyst (reaction slow without AlCl <sub>3</sub> )	IICl, SO <sub>2</sub> , S
H <sub>2</sub> SO <sub>4</sub>	—	ClSO <sub>3</sub> H or S <sub>2</sub> O <sub>5</sub> Cl <sub>2</sub> , SO <sub>2</sub> , HCl
SO <sub>3</sub>	100°C.	S <sub>2</sub> O <sub>5</sub> Cl <sub>2</sub>
HNO <sub>3</sub>	—	H <sub>2</sub> SO <sub>4</sub> , NO <sub>2</sub> Cl, NOCl
AgNO <sub>3</sub>	Dry reaction	NO <sub>2</sub> SO <sub>2</sub> Cl, AgCl
N <sub>2</sub> O <sub>4</sub>	—	NOCl, SO <sub>2</sub>
HBr	–80°C.	SOBr <sub>2</sub> , HCl
HI	—	I <sub>2</sub> , HCl, SO <sub>2</sub> , S
NH <sub>3</sub>	Vapor-phase reaction	HCl + HNSO (b.p. –85°C.) (29a)

Thionyl chloride reacts with organic compounds containing hydroxy groups to form the corresponding chlorides. Thus, its reaction with alcohols or phenols produces the corresponding chloro compounds. With organic acids, either acid chlorides or acid anhydrides are formed, depending upon the ratio of acid to thionyl chloride. Equimolal quantities of acid and thionyl chloride yield the acid chloride, but when the ratio of acid to thionyl chloride is 2:1 the acid anhydride is obtained. Reactions with sulfonic acids yield sulfonyl chlorides.

The reaction of thionyl chloride with a Grignard reagent yields the corresponding sulfoxide:



Ionic reactions with thionyl chloride as solvent have been studied (31a).

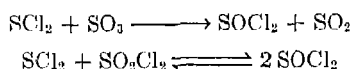
#### MANUFACTURE

Thionyl chloride was first obtained by Persoz and Bloch in 1849 by the interaction of sulfur dioxide and phosphorus pentachloride:

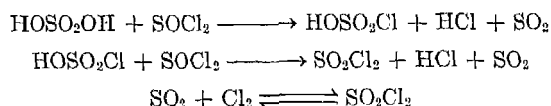


The thionyl chloride may be obtained with some difficulty from the reaction mass by fractional distillation.

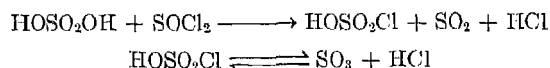
Most commercial methods of preparation, however, are based upon the oxidation of sulfur dichloride either with sulfur trioxide or sulfuryl chloride:



A variety of starting materials may be used for these reactions. The sulfur dichloride is usually produced directly in the reactor by reaction of chlorine with either sulfur or sulfur monochloride. The sulfuryl chloride results either from the chlorination of sulfur dioxide or from the chlorination of sulfuric acid with part of the thionyl chloride produced:

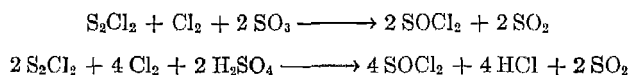


The sulfur trioxide may either be introduced into the reactor as such, as oleum, or may be derived from the sulfuric acid:



It will be seen that these reactions permit a fairly wide variety of raw materials to be used in the manufacture of thionyl chloride, with the result that several related processes have been developed for the manufacture of this chemical.

In the process patented by Hooker Electrochemical Co. (40), the reaction is carried out in a glass-lined, jacketed, iron vessel fitted with an agitator, and a condenser arranged either for reflux or for distillation. The vessel may be charged with either sulfur monochloride or sulfur dichloride and about 1% of antimony trichloride as a catalyst. Chlorine is introduced into the reactor near its bottom. Liquid oleum of as high a free  $\text{SO}_3$  concentration as is practical, usually around 70% free  $\text{SO}_3$ , is added to the reactor at such a rate that the temperature of the reaction mass is held at around  $25^\circ\text{C}$ . The use of cooling water in the jacket of the reactor helps to speed the reaction by cooling the mass. When the batch has been completed a slight excess of oleum and chlorine are added to reduce to a minimum the residual  $\text{SCl}_2$ . The reaction can be written as a combination of the equations:

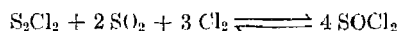


Inasmuch as thionyl chloride combines readily with sulfur trioxide to form the relatively stable pyrosulfuryl chloride, it is essential to maintain the concentration of sulfur trioxide in the reaction mass at a low level. Hence, the addition of oleum to sulfur chloride rather than the reverse operation. Correspondingly, low temperatures are employed to minimize formation of the higher oxides. When all of the reactants have been added, heat is applied to the jacket of the reactor and the batch is refluxed until most of the sulfur dioxide, hydrogen chloride, chlorine, etc., have been eliminated. The thionyl chloride is then distilled from the reactor (leaving the high-boiling oxides and other impurities) and further purified if necessary. A batch requires from 45 to 50 hours of processing time.



In the process as patented by E. I. du Pont de Nemours & Co. (41), the reaction is operated on a continuous basis at a temperature between 105° and 110°C. The reactor contains a heel of sulfur monochloride with about 1% of antimony trichloride as catalyst. A mixture of sulfur trioxide vapor and an excess of chlorine are introduced into the reactor near its bottom. The thionyl chloride and sulfur dioxide which are formed by the reaction together with the excess chlorine, any unreacted sulfur trioxide, and a substantial quantity of vaporized sulfur monochloride rise from the reactor. The excess chlorine is recovered in a sulfur-sulfur chloride scrubber and is returned to the reactor. The thionyl chloride is separated from the sulfur monochloride in a fractionating column. The sulfur monochloride is returned to the reactor. By maintaining a low (3-15%) concentration of thionyl chloride in the reactor as well as a low concentration of sulfur trioxide the formation of pyrosulfuryl chloride is minimized, and a continuous operation is achieved. Yields of thionyl chloride by this process are around 92%, based on the chlorine and sulfur. Reaction rates of between 5 and 6 lb. of thionyl chloride per gallon of reaction heel volume per hour are experienced.

In the process patented by Pittsburgh Plate Glass Co. (42) sulfur monochloride, sulfur dioxide, and chlorine are reacted at around 200°C. in the presence of an activated carbon catalyst to produce thionyl chloride:

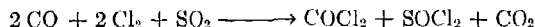


Using a 0-10% excess of chlorine and about 100% excess of sulfur dioxide, conversions of around 50% are obtained. The liquids in the reaction product are condensed, and separated, the sulfur mono- and dichloride being returned for further reaction. The excess gases are likewise recycled. This process has the advantage that it produces an ultimate yield of near 100% on all of the reactants.

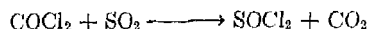
The process, patented by Allied Chemical & Dye Corp. (43), is based upon the reaction:



In this process, sulfur dioxide, chlorine, and carbon monoxide are brought together in the presence of activated wood charcoal at carefully controlled temperatures, in the first stage at 170°C. and in the second stage at 200°C. in such a manner as to minimize the formation of either sulfur chlorides or sulfuryl chloride. The reaction is:



The thionyl chloride condensed out of the reaction gases from these stages is of high purity, containing only a trace of either sulfur chloride or sulfuryl chloride. To the phosgene remaining in the noncondensable fraction is added an excess of sulfur dioxide and the mixture is passed through a third reaction chamber maintained at 310°C. The reaction taking place in this reactor is:



The products from the third reactor are condensed at -30°C. to remove all but the carbon dioxide. A technical grade of thionyl chloride is obtained upon fractionation of this condensate.

Thionyl chloride is a hazardous chemical. Its vapors are irritating to the eyes and mucous membranes. The liquid is corrosive to the skin. In handling thionyl chloride, the care usual in the handling of volatile, corrosive, and toxic materials must be

exercised; one part of water reacts with about seven parts of thionyl chloride so contact with water or moist air must be avoided in storage and handling. Storage tanks should be furnished with vents modified to contain drying agents to prevent suck-back of moist air. Drums of thionyl chloride should be tightly sealed, but should be periodically vented to relieve any pressure which may develop. Lead, nickel, or glass equipment may be used in handling thionyl chloride; iron can be used, but it is not completely free from attack.

Thionyl chloride is produced in the technical and refined grades. Typical analyses and boiling ranges of these are given in Table IX.

TABLE IX. Analysis of Technical and Refined Thionyl Chloride.

Analysis	Technical grade	Refined grade
SOCl <sub>2</sub> .....	93+%	97.5%
SO <sub>2</sub> .....	0.7%	0.5%
S <sub>2</sub> Cl <sub>2</sub> .....	1.5%	0.5%
SO <sub>2</sub> Cl <sub>2</sub> .....	±.5%	1.5%
Fe.....		20 p.p.m.
Boiling range.....	72-79°C.	75-78°C.

#### USES

Thionyl chloride is extensively used in organic synthesis to replace various groups, particularly hydroxy groups, with chlorine. It is used in the preparation of fatty acid chlorides which in turn are reacted to form a variety of surface-active agents. It finds use also in the preparation of pharmaceuticals and of dyes. The following are some of the end products prepared through the use of thionyl chloride: isoamyl chloride, synthetic pyrethrum, synthetic vitamin A palmitate, and antihistamines.

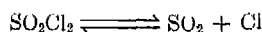
Because of its extreme reactivity with water and because the products of its hydrolysis are gases, thionyl chloride has been suggested as a dehydrating agent for removing the last traces of water of hydration from difficultly dehydratable salts such as MgCl<sub>2</sub>·6H<sub>2</sub>O, FeCl<sub>3</sub>·4H<sub>2</sub>O, AlCl<sub>3</sub>·6H<sub>2</sub>O, TiCl<sub>3</sub>, etc.

#### Sulfuryl Chloride.

Sulfuryl chloride (sulfuric oxychloride), SO<sub>2</sub>Cl<sub>2</sub>, formula weight 134.98, is a colorless liquid with an extremely pungent odor. M.p. -46°C.; b.p. 69.1°C.;  $d_4^{20}$  1.6674;  $n_D^{20}$  1.443; sp. heat 0.233 cal./gram; latent heat of vaporization 49.5 cal./gram; heat of formation 89.540 cal./gram-mole; ebullioscopic constant 45; coefficient of cubical expansion 0.0012/°C.; viscosity 0.918 cps. at 0°C., 0.1596 at 38°C.; vapor pressure 40.9 mm. at 0°C., 95.2 mm. at 18°C., 745 mm. at 68.7°C.; dielectric constant at 22°C. 9.15; electrical conductivity at 25°C.  $3 \times 10^{-8}$  (mho)(cm.)/(sq.cm.).

Sulfuryl chloride is a solvent for many substances, including sulfur dioxide, iodine, bromine, iron chloride, iodides of mercury, cadmium, arsenic, tin, and the substituted ammonium radicals. Solutions of most salts in sulfuryl chloride are only slightly conductive, but solutions of tertiary or quaternary ammonium salts are considerably dissociated and conduct well. Sulfuryl chloride is miscible with organic solvents, including acetic acid and ether.

Sulfuryl chloride is stable at room temperature, but it decomposes at elevated temperatures:



The equilibrium constant for the reaction in the vapor phase,  $K = p(\text{SO}_2) p(\text{Cl}_2)/p(\text{SO}_2\text{Cl}_2)$ , is given below for various temperatures:

Temperature, °C.....	30	40	50	102	159	191
$K$ .....	0.0288	0.0506	0.0837	2.37	8.9	13.1

The decomposition of sulfuryl chloride is photochemically accelerated. It is also catalyzed by a variety of materials, including aluminum chloride, activated charcoal, glass, etc.

The ease with which sulfuryl chloride decomposes into sulfur dioxide and chlorine, particularly in the presence of catalysts, explains at least partially many of its reactions. Thus, it reacts with sulfur at 200°C., or at room temperature in the presence of aluminum chloride, to form sulfur monochloride and sulfur dioxide:

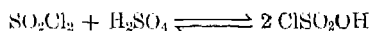


With hydrogen sulfide, it forms a variety of products, including hydrogen chloride, sulfur monochloride, sulfur, sulfur dioxide, etc. Sulfuryl chloride liberates bromine or iodine from bromides or iodides, and breaks down into the corresponding chloride and sulfur dioxide.

Sulfuryl chloride is hydrolyzed very slowly by cold water:



With controlled quantities of water or with sulfuric acid directly, it is converted to chlorosulfonic acid:

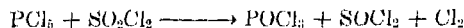


This reaction, however, is reversed at boiling temperatures. In the presence of a mercuric salt, it is possible to fractionate sulfuryl chloride from boiling chlorosulfonic acid.

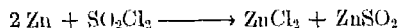
Iodine reacts with sulfuryl chloride in the presence of aluminum chloride to form iodine chlorides:



Phosphorus chlorides react with sulfuryl chloride:



In ether solution, zinc reacts with sulfuryl chloride to yield the chloride and sulfoxylate:



Metal oxides react to form the chlorides and sulfates. Metal sulfides may be chloridized with sulfuryl chloride.

Sulfuryl chloride reacts with anhydrous ammonia to yield a variety of sulfamides having the general formula:  $\text{NH}_2\text{SO}_2(\text{NHSO}_2)_n\text{NH}_2$  where  $n$  may vary from 0 up. Cyclic compounds of the formula  $(\text{SO}_2\text{NH})_3$  are also produced.

In organic chemistry, sulfuryl chloride is a chlorinating agent and a sulfonating agent. As a chlorinating agent, it in many cases parallels the action of elementary chlorine. However, by careful selection of reaction conditions and catalyst it is often possible to obtain more selective chlorination with sulfuryl chloride than with chlorine

itself. Thus, *m*-cresol is chlorinated in the para position with sulfuryl chloride to yield a disinfectant. Thymol is similarly selectively chlorinated in commercial operation. A variety of aromatics may be chlorinated in a stepwise manner with sulfuryl chloride. In these reactions, aluminum chloride is sometimes used as a catalyst.

Sulfuryl chloride reacts with sodium salts of organic acids to form the corresponding acid chlorides. Acetyl chloride may be prepared in this manner:



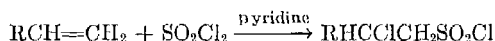
By varying the conditions of the reaction, the acid anhydride may be formed. The by-product sulfuric acid or sodium sulfate tends to introduce oxidation reactions which reduce the yield.

Sulfuryl chloride reacts with ethyl alcohol to yield ethyl chlorosulfonate:

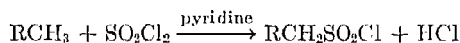


The use of organic peroxides as catalysts permits the chlorination of aliphatic hydrocarbons and their derivatives. Thus toluene is chlorinated in the side chain, first to benzyl chloride and then to benzal chloride. Alkenes are chlorinated to saturated dichlorides with sulfuryl chloride in the presence of organic peroxides as catalysts. Correspondingly, organic acids and acid chlorides may be chlorinated in various positions. Benzaldehyde under these conditions is chlorinated to benzoyl chloride.

The use of pyridine as a catalyst causes the formation of sulfonyl chlorides. Thus, with alkenes:

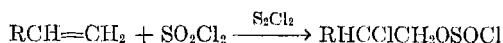


Or with saturated hydrocarbons:



Besides pyridine, a number of other compounds catalyze this reaction. Thus, triethanolamine or benzonitrile, may under certain circumstances be used to catalyze the chlorosulfonation of saturated hydrocarbons. This reaction is useful in the preparation of surfactants from petroleum products, and in the preparation of some types of tanning agents.

When sulfuryl chloride is reacted with alkenes using sulfur monochloride as the catalyst, chlorosulfites are formed:



Sulfuryl chloride is prepared by the reaction of dry sulfur dioxide with chlorine in the presence of an active carbon catalyst. The reaction is carried out in a steel vessel with water-cooled walls so arranged that the catalyst is wetted with the sulfuryl chloride being formed. The product is condensed in a steel condenser.

A number of organic compounds may replace the active carbon as a catalyst. Thus, camphor may be dissolved in liquid sulfur dioxide, and chlorine then passed through the resulting clear solution at about 0°C. The sulfuryl chloride so formed may be distilled from the reaction mass. Terpene hydrocarbons, certain ethers, phenols, and esters are also effective catalysts.

Sulfuryl chloride is a hazardous chemical. Its vapor is highly toxic and the liquid is corrosive to the skin. It is therefore essential to follow the usual precautions in handling a volatile liquid of this type, avoiding contact of the liquid with the skin or

clothing. In case of contact with the skin or eyes, immediately flush with plenty of water for at least 15 minutes. Medical attention is required if the liquid touches the eyes.

Sulfuryl chloride, if completely dry, does not corrode aluminum, magnesium, or nickel at room temperature. It slightly corrodes chrome steel, iron, cast iron, lead, zinc, aluminum bronze, and German silver, and rapidly corrodes copper and brass. Moisture considerably increases corrosion, but the increased attack on lead is less than with other metals. Dry sulfuryl chloride may be handled in iron or steel equipment, but lead, glass, or nickel equipment are preferred because of their greater resistance to corrosion.

Since moisture in contact with sulfuryl chloride causes the liberation of hydrogen chloride, it is necessary to vent storage containers at frequent intervals to prevent undue build-up of pressure. Correspondingly, it is essential to protect the sulfuryl chloride from attack by atmospheric moisture. It follows also that empty drums must not be washed out with water or used for other purposes. The use of pressure to empty a drum of sulfuryl chloride is hazardous. Since light catalyzes decomposition, carboys or other glass containers of sulfuryl chloride should be kept out of the sun and away from heat.

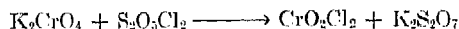
The commercial material is a pale yellow liquid with a distillation range of 2°C. (including 69.5°C.). It contains at least 99% sulfuryl chloride.

Sulfuryl chloride is primarily a chlorinating or chlorosulfonating agent. It is used to convert organic acids to the corresponding acid chlorides and acid anhydrides. It is used as a selective chlorinating agent particularly in the production of chlorophenol and chlorothymol, which are used as disinfectants. It is also used in the syntheses of various pharmaceuticals, dyes, and surfactants.

### Pyrosulfuryl Chloride.

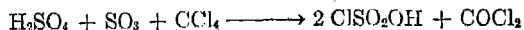
Pyrosulfuryl chloride (disulfuryl chloride),  $\text{S}_2\text{O}_5\text{Cl}_2$ , formula weight 215.05, is a colorless, dense, somewhat viscous liquid. M.p.  $-37^\circ\text{C}$ .; b.p.  $152^\circ\text{C}$ .;  $d_4^{20}$  1.837;  $n_D^{19}$  1.449; heat of vaporization 35.1 cal./gram.

At room temperature, pyrosulfuryl chloride is fairly stable. However, at temperatures over  $180^\circ\text{C}$ . it decomposes into sulfur dioxide, sulfur trioxide, and chlorine. At  $360^\circ\text{C}$ ., its decomposition is virtually complete. Pyrosulfuryl chloride is slowly attacked by water, sulfuric and hydrochloric acids resulting. If the pyrosulfuryl chloride is in excess, some chlorine and sulfur dioxide are also formed. Pyrosulfuryl chloride reacts with chromates to form chromyl chloride:

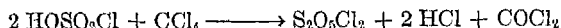


Pyrosulfuryl chloride may be prepared by the chlorination of sulfur trioxide with a wide range of chlorides.  $\text{S}_2\text{Cl}_2$ ,  $\text{SOCl}_2$ ,  $\text{PCl}_5$ ,  $\text{POCl}_3$ ,  $\text{SiCl}_4$ ,  $\text{Si}_2\text{OCl}_6$ ,  $\text{NaCl}$ , and  $\text{CCl}_4$  have all been reported to have converted sulfur trioxide to pyrosulfuryl chloride. Strangely enough, however, pyrosulfuryl chloride cannot be prepared by refluxing together sulfuryl chloride and sulfur trioxide. Pyrosulfuryl chloride may also be obtained by dehydrating chlorosulfonic acid with phosphorus pentoxide or pentachloride.

The usual method for preparing pyrosulfuryl chloride is to add oleum to hot carbon tetrachloride:



This reaction is immediately followed by:

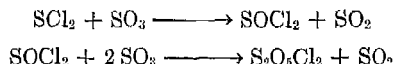


The reaction mass is treated with dry sodium chloride to remove any unreacted chlorosulfonic acid (as sodium chlorosulfonate) and is then fractionally distilled to obtain a refined pyrosulfuryl chloride. This process has the disadvantage that extremely poisonous phosgene is produced as a by-product.

Another process used for the production of pyrosulfuryl chloride involves the reaction between sulfur monochloride and sulfur trioxide. In this process, which is operated on a batch basis, sulfur monochloride is added slowly to liquid sulfur trioxide at a temperature of 35°C. until 85 to 95% of the sulfur trioxide has been reacted. The batch is then fractionally distilled to remove sulfur dioxide, unreacted sulfur trioxide, and traces of sulfur chlorides. The net reaction is:



A third process involves the reaction of sulfur trioxide vapor with sulfur dichloride in a heel of pyrosulfuryl chloride held at around 110°C. The reactor is fitted with a reflux condenser to return any reactants or intermediates which may have vaporized from the reaction mass. The pyrosulfuryl chloride produced is collected in the reactor. The crude product is fractionally distilled to remove sulfur dioxide, sulfur trioxide, sulfur dichloride, and thionyl chloride. A product purity of 99% is obtained. The reactions are:



Any sulfuric acid introduced into the reactor forms chlorosulfonic acid. This material forms an azeotrope with the pyrosulfuryl chloride, which is difficult to separate. Hence it is essential to minimize the sulfuric acid carry-over if the sulfur trioxide is obtained from oleum.

Pyrosulfuryl chloride is useful as a chlorinating agent in organic chemistry.

### Sulfur Oxytetrachloride.

Sulfur oxytetrachloride ("trichlorosulfonium chlorosulfonate"),  $\text{S}_2\text{O}_3\text{Cl}_4$ , formula weight 253.96, is a pungent, colorless, crystalline solid that melts at about 57°C. with decomposition. It is formed by the action of sulfur tetrachloride on chlorosulfonic acid at  $-15^\circ\text{C}$ . or lower:



It slowly decomposes at room temperature to thionyl chloride and sulfuryl chloride. Sulfur oxytetrachloride hydrolyzes to sulfurous acid, sulfuric acid, and hydrochloric acid. It is believed to be the trichlorosulfonium salt of chlorosulfonic acid.

### Sulfur Nitrides.

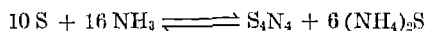
Nitrogen combines with sulfur to form at least three sulfur nitrides,  $\text{S}_4\text{N}_4$ ,  $\text{S}_6\text{N}_2$ , and  $\text{S}_2\text{N}$ . These nitrides have often been called nitrogen sulfides, but chemical evidence indicates that they are nitrides rather than sulfides. For example, on hydrolysis they yield ammonia. These compounds in turn react with various other reagents to form a rather large family of derivatives that have not been extensively studied.

**Tetrasulfur tetranitride** (tetranitrogen tetrasulfide, nitrogen sulfide),  $S_4N_4$ , formula weight 184.27, is an orange-red crystalline solid, m.p. 179°C. (with sublimation at about the same temperature);  $d_{25}^{15}$  2.22. The solid is highly explosive at elevated temperatures and will detonate when struck, even at room temperature (see Vol. 6, p. 19). It is slowly decomposed by water but is soluble in organic solvents. Its solubility in several of these solvents is listed in Table X.

TABLE X. Solubility of Tetrasulfur Tetranitride in Organic Solvents.

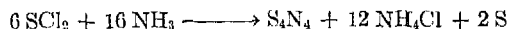
Temperature, °C.	Solubility, grams per liter		
	$CS_2$	$C_6H_6$	$C_2H_5OH$
0	3.705	2.266	0.645
10	6.845	4.260	0.830
20	9.391	6.301	1.050
30	13.188	8.692	1.271
40	16.887	11.107	1.478
50	—	13.721	1.640
60	—	17.100	—

Tetrasulfur tetranitride is formed by the reaction of sulfur with dry ammonia through a rather complex series of reversible reactions. The overall reaction is given by the equation:



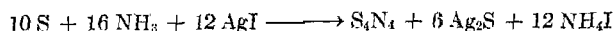
The equilibrium for this reaction appears to be predominantly toward the left of this equation. In order to recover tetrasulfur tetranitride, it is therefore necessary to remove the ammonium sulfide as it is formed. This may be accomplished by oxidation (with chlorine or other reagents) or by precipitation with silver ion or other sulfide insoluble cation. Since the tetrasulfur tetranitride is readily hydrolyzed by water, the reaction must be carried out in an anhydrous medium. The reactions most frequently used to prepare tetrasulfur tetranitride are:

(1) The reaction of dry ammonia gas (usually diluted with air) with an ice-cold 10 to 12% solution of  $SCl_2$  in benzene:



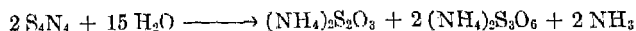
The products of reaction are largely insoluble in benzene and the tetrasulfur tetranitride is recovered from the precipitate by fractional crystallization. The mother liquor contains, in addition to some dissolved tetrasulfur tetranitride and sulfur, a variety of other by-products including  $N_4H_4SCl_2$  and  $N_4H_4Cl_4$ .

(2) The reaction of sulfur with an excess of liquid ammonia in the presence of silver iodide:



The tetrasulfur tetranitride, which is soluble in ammonia, is obtained by evaporation of the filtrate from the reaction mass. Again, the progress of the reaction is complex and numerous intermediates are formed. Among these,  $S(NH_3)_3$  and  $S(NH_3)_6$  have been reported.

Tetrasulfur tetranitride is not wetted with water, hence it hydrolyzes rather slowly in cold water. The hydrolysis reaction is:



In the presence of alkalis, the hydrolysis is as follows:



Dry hydrogen chloride reacts with tetrasulfur tetranitride to produce as primary products ammonia, sulfur, and chlorine. Hydrogen sulfide reduces tetrasulfur tetranitride in benzene solution to ammonium polysulfide. Some of the reactions of tetrasulfur tetranitride are listed in Table XI.

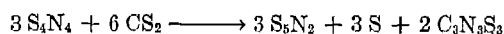
TABLE XI. Some Reactions of Tetrasulfur Tetranitride.

Reactant	Conditions	Product	Product properties
$\text{CS}_2$	Heat and pressure	$\text{S}_5\text{N}_2$ , pentasulfur dinitride	See Vol. 3, p. 142.
Sulfur	125°C.	$\text{S}_2\text{N}_2$ , disulfur nitride	Dark red liquid with penetrating iodine-like odor. Dec. into $\text{S}_4\text{N}_4$ . Hydrolyzes to sulfur and ammonium salt.
$\text{Cl}_2$	In org. solvent	$\text{N}_4\text{S}_4\text{Cl}_4$ , nitrogen chlorosulfide	Yellow cryst. solid. Dec. rapidly at 100°C. to form $\text{S}_2\text{Cl}_2$ , $\text{N}_2$ , and $\text{N}_3\text{S}_3\text{Cl}$ (trithiazyl chloride). Hydrolyzes to $\text{NH}_4\text{Cl}$ and $\text{SO}_2$ .
$\text{SCl}_2$	In boiling $\text{CCl}_4$	$\text{N}_3\text{S}_4\text{Cl}$ , thiotrithiazyl chloride	Yellow cryst. solid slightly sol. in thionyl chloride. Decomposed by water to $(\text{NH}_4)_2\text{S}_3\text{O}_6$ , $\text{NH}_4\text{Cl}$ , and S. The chloride may be replaced by other anions such as $\text{NO}_3^-$ , $\text{HSO}_4^-$ , $\text{I}^-$ , $\text{Br}^-$ , $\text{CNS}^-$ , etc. It reacts with ammonia to form an explosive material.
$\text{S}_2\text{Cl}_2$	Cold	$\text{N}_3\text{S}_6\text{Cl}_2$ , dithiotetra-thiazyl chloride	Black crystals that dec. on heating to $\text{N}_3\text{S}_4\text{Cl}$ .
$\text{Br}_2$	—	$\text{N}_4\text{S}_4\text{Br}_4$ , nitrogen bromosulfide	Bronze-colored crystals.
$\text{S}_2\text{Br}_2$	$\text{CS}_2$ soln.	$\text{N}_3\text{S}_4\text{Br}$ , thiotrithiazyl bromide	Yellow needle-like crystals.
$\text{PbI}_2$	In liquid $\text{NH}_3$	$\text{PbN}_2\text{S}_2\text{NH}_3$	Olive-green prisms.
$\text{HgI}_2$	In liquid $\text{NH}_3$	$\text{HgN}_2\text{S}_2\text{NH}_3$	—

Tetrasulfur tetranitride forms addition compounds with many chemicals,  $\text{S}_4\text{N}_4 \cdot \text{TiCl}_4$ ,  $\text{S}_4\text{N}_4 \cdot \text{SbCl}_5$ ,  $2\text{S}_4\text{N}_4 \cdot \text{SnCl}_4$ ,  $\text{S}_4\text{N}_4 \cdot \text{SeCl}_2$ ,  $\text{S}_4\text{N}_4 \cdot \text{WCl}_6$ ,  $3\text{S}_4\text{N}_4 \cdot 2\text{SCl}_2$ ,  $\text{S}_4\text{N}_4 \cdot \text{SCl}_2$ , and  $\text{S}_4\text{N}_4 \cdot 2\text{SCl}_2$  having been reported.

Tetrasulfur tetranitride has been suggested for use as an insecticide.

**Pentasulfur dinitride** (nitrogen pentasulfide),  $\text{S}_5\text{N}_2$ , formula weight 188.32, is a deep red liquid with a strong disagreeable odor; m.p. 10°C.;  $d_{20}^{18}$  1.901. It is obtained by heating tetrasulfur tetranitride with carbon disulfide at 100°C. for several hours. The reaction is:



The pentasulfur dinitride, which is soluble in carbon disulfide, is recovered by filtering off the precipitated  $\text{C}_3\text{N}_3\text{S}_3$ , followed by fractional crystallization.

Pentasulfur dinitride decomposes, upon heating, into sulfur and nitrogen. It reacts slowly with water. Among the products of its hydrolysis are ammonia and sulfur. Its reaction with alkali in alcoholic solution produces a transient but intense



violet-red color that is characteristic of this material and may be used in its detection. Solutions of pentasulfur dinitride are decomposed by light into tetrasulfur tetranitride and sulfur.

**Disulfur nitride** (nitrogen disulfide, nitrogen persulfide),  $S_2N$ , formula weight 78.14, is a red liquid resembling liquid bromine, but having a penetrating odor resembling that of iodine. It is moderately volatile and is soluble in benzene, chloroform, carbon bisulfide, and ether. It slowly decomposes at room temperature to  $S_4N_4$  and sulfur. It is hydrolyzed to sulfur and ammonium salts.

Disulfur nitride is obtained by the reaction of  $S_4N_4$  and sulfur at  $125^\circ C.$ , the product being condensed from the gases evolved. A compound of similar composition has been obtained by the action of active nitrogen (produced through the action of a silent electric discharge between aluminum electrodes) on sulfur. The product so obtained is initially a black solid but is converted to the red liquid by heating.

### Sulfur Oxides.

A large number of oxides of sulfur have been reported, described, or prepared (30,33). These include  $S_2O$ ,  $SO$ ,  $S_2O_2$ ,  $S_2O_3$ ,  $SO_2$ ,  $SO_3$ ,  $S_2O_7$ ,  $SO_4$ , and  $S_2O_8$  as well as various polymers of  $SO_3$ . Of these, only the dioxide,  $SO_2$ , and the trioxide,  $SO_3$  (see *Sulfuric acid*), are commercial and well known.  $S_2O$  is doubtful, as is  $S_2O_7$ .  $S_2O_2$  and  $S_2O_8$  are doubtful dimers of  $SO$  and  $SO_4$  (7).

**Sulfur monoxide**,  $SO$ , is known largely through the work of F. W. Schenk from 1933 to the present. It is known only as a gas which is stable for several days at room temperatures. Sulfur monoxide can be prepared by several methods, the best of which is passage through an electric discharge of sulfur vapor and sulfur dioxide at low pressures and at about  $175^\circ C.$  It can also be formed in small yields by the action of silver on thionyl chloride or bromide at about  $150^\circ C.$  The gas polymerizes irreversibly upon compression or cooling to an orange-red solid, which decomposes on heating to the monoxide, the dioxide, and sulfur. Sulfur monoxide can be detected by its characteristic absorption bands extending from 3130 Å. to the shorter wave lengths. It has the same spectral ground state as oxygen and  $S_2$  and hence is probably paramagnetic like the latter two gases. Its dissociation energy is also intermediate between diatomic sulfur and oxygen. Upon hydrolysis, both sulfur and dithionite ion are obtained.

**Disulfur trioxide** (sulfur sesquioxide),  $S_2O_3$ , is a blue to blue-green solid prepared by the addition of powdered sulfur to liquid sulfur trioxide at  $15^\circ C.$  The product is undoubtedly a polymer of  $S_2O_3$  and slowly decomposes on standing in air to the trioxide, the dioxide, and sulfur.

**Sulfur tetroxide**,  $SO_4$ , is a white solid formed by subjecting a mixture of dry sulfur dioxide and oxygen to a silent electric discharge. It is a powerful oxidizing agent that melts at about  $3^\circ C.$  with some decomposition. Its structure is unknown.

### Sulfur Dioxide.

Owing to the wide occurrence and peculiar properties of sulfur and sulfides, sulfur dioxide fumes have been known and utilized since earliest recorded history. Homer refers to its use as a disinfectant and the bleaching of linen with the fumes of burning sulfur was known and practiced as early as 2000 B.C. in Egypt. With the development of modern industrial civilization and its demand for metals, sulfuric acid, and

wood pulp, sulfur dioxide achieved great technical importance far exceeding its minor and more recent development as a pure commercial chemical.

Sulfur dioxide is one of the very minor and variable constituents of the atmosphere. Volcanic and other terrigenous gases contain on the order of 10% of sulfur-containing gases, largely sulfur dioxide and hydrogen sulfide. In some areas the amount of sulfur dioxide in the atmosphere is increasing and reaches measurable concentrations as the result of heavy and widespread industrial activity (22). It has been estimated that, during World War II, about 75,000,000 tons of sulfur dioxide was released to the atmosphere annually in the U.S. in the form of waste gases from various sources (23).

The sources and disposition of sulfur dioxide are quite varied. The most economic and important source is elemental sulfur. Most of the Frasch process sulfur produced in this country is burned to make sulfur dioxide. Practically all of this is consumed immediately in the manufacture of sulfuric acid, sulfite pulp, and other captive uses. Most of the liquid sulfur dioxide made originates from this source. Smelter gases are a large and relatively concentrated source of sulfur dioxide, which is largely wasted to the atmosphere, although a small but increasing percentage is being recovered as sulfuric acid and liquid sulfur dioxide. For several years up to 1943 some sulfur dioxide from this source was recovered as elemental sulfur in Canada and Europe, but this was abandoned because of the increasing cost of coke used in the reduction. Another source of sulfur dioxide is the combustion of hydrogen sulfide from oil refining, coke oven operation, and the refining of natural and manufactured gas. Most of it is wasted to the atmosphere, but in recent years the recovery of the sulfur content of these wastes as either sulfuric acid or elemental sulfur has grown rapidly. The widespread combustion of fuels, such as petroleum oil, natural and manufactured gases, and coal, particularly the latter, produces enormous quantities of sulfur dioxide in the form of dilute flue gases, which are vented to the atmosphere. In some very large power plants in some communities, notably in English urban districts (23), removal of sulfur dioxide from gases at levels as low as 0.02 to 0.05% initial sulfur dioxide content has proved necessary, and in more recent years the recovery of over 90% of the sulfur values in these dilute gases has been studied on a pilot plant scale.

#### PROPERTIES

Sulfur dioxide is a colorless gas with a characteristic pungent choking odor. It condenses at  $-10^{\circ}\text{C}.$  at atmospheric pressure to a colorless liquid that freezes at  $-75.5^{\circ}\text{C}.$  The molecular formula is  $\text{SO}_2$ , corresponding to a molecular weight of 64.06 in all its states. The critical temperature is  $157.12^{\circ}\text{C}.$  and the critical pressure is 77.65 atm. At  $0^{\circ}\text{C}.$  and 1 atm. pressure, the gas has a specific gravity of 2.2636 relative to air, occupies 5.47 cu.ft./lb., has a specific heat of 0.15 cal./gram and a dielectric constant of 1.0095. It has discontinuous absorption bands in the ultra-violet region.

For the liquid at  $20^{\circ}\text{C}.$ ,  $d_{15.6}^{20} = 1.4542$ ,  $C_p = 0.327$  cal./gram, the dielectric constant is 12.8,  $n_D^{20} = 1.410$ , the surface tension is 22.73 dynes/cm.; the latent heat of vaporization is 149 B.t.u./lb.; and its viscosity is 0.28 cps.

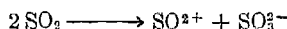
Liquid sulfur dioxide expands about 10% in volume in going from 20 to  $60^{\circ}\text{C}.$  The pure liquid is a poor conductor of electricity, although solutions of a limited number of salts that are soluble in sulfur dioxide exhibit high conductivity. Liquid sulfur dioxide is only slightly miscible with water, is a nonsolvent for sulfur, and is miscible in all proportions with sulfur monochloride. The gas is soluble to the extent of 36

volumes in water at 20°C., but is very much more soluble in a number of organic solvents, such as camphor, acetone, and formic acid. One volume of the latter solvents will dissolve several hundred volumes of sulfur dioxide.

Sulfur dioxide is a relatively inert and stable gas that can be heated to above 2000°C. without appreciable decomposition. It does not form flammable or explosive mixtures with air. Its stability is indicated by its high heat and free energy of formation, which are 70.9 and -69.7 kg.-cal./mole, respectively. Sulfur dioxide gas undergoes addition reactions with gaseous or solid halogens:  $\text{SO}_2 + \text{X}_2 = \text{SO}_2\text{X}_2$ . Reduction of the gas can be carried out with reducing agents such as hydrogen, hydrogen sulfide, carbon monoxide, and carbon at temperatures up to 1000°C., to sulfur and water or carbon dioxide as the case may be. Reaction takes place at a much lower temperature if a catalyst, such as bauxite, is used. The oxidation of sulfur dioxide to the trioxide has been the subject of considerable study (see *Sulfuric acid*). It is generally carried out in the presence of a catalyst at temperatures in the range of 400 to 700°C.

Sulfur dioxide is readily formed by the air oxidation of sulfur and many sulfides, by the pyrolysis in air of sulfites and thiosulfates, by the reduction of sulfur trioxide and sulfuric acid by metals, carbon, sulfur, and sulfides with heating, and by the decomposition of sulfite and bisulfite solutions with strong acids.

Liquid sulfur dioxide or the gas at low temperatures forms solid complex salts with solid iodides and thiocyanates and other salts. The addition compounds contain from  $\frac{1}{2}$  to 4 moles of sulfur dioxide and form conducting solutions in liquid sulfur dioxide. Reactions in liquid sulfur dioxide are considered (21) to depend on its ionization:



corresponding to  $2\text{H}_2\text{O} \rightarrow \text{H}_3\text{O}^+ + \text{OH}^-$  in water. Thus, in liquid sulfur dioxide, thionyl chloride can be considered to be an acid  $\text{SOCl}_2 \rightarrow \text{SO}^{2+} + 2\text{Cl}^-$  and sodium sulfite; and  $\text{Na}_2\text{SO}_3 \rightarrow 2\text{Na}^+ + \text{SO}_3^{2-}$  a base, which react to form a salt:  $\text{Na}_2\text{SO}_3 + \text{SOCl}_2 \rightarrow 2\text{NaCl} + 2\text{SO}_2$ . See also *Acid-base systems*.

**Sulfurous Acid.** Sulfur dioxide dissolves in water to form the weak acid, sulfurous acid,  $\text{H}_2\text{SO}_3$ . At a partial pressure for sulfur dioxide gas of 1 atm., solutions containing 18.5%  $\text{SO}_2$  by weight are formed at 0°C. and 5.1% strength at 40°C. Under practical conditions, where solutions are formed most often at 1 atm. total pressure with air or other diluent gases present, concentrations of from only  $\frac{1}{3}$  to  $\frac{1}{2}$  of these values are obtained. At 25°C. the first and second ionization constants of sulfurous acid in water are  $1.72 \times 10^{-2}$  and  $1.1 \times 10^{-9}$ , respectively. Free sulfurous acid has not been prepared, although a hydrate  $\text{SO}_2 \cdot 7\text{H}_2\text{O}$  has been isolated from concentrated solutions at low temperatures.

Sulfites are first formed by the absorption of sulfur dioxide in alkaline solutions followed by the formation of even more soluble bisulfites as absorption of sulfur dioxide continues. In addition to these simple salts,  $\text{M}_2\text{SO}_3$  and  $\text{MHSO}_3$ , a series of alkali metal "pyro" salts,  $\text{M}_2\text{S}_2\text{O}_5$ , also exists. These may be considered anhydrides of the bisulfites and are formed by heating the bisulfites or their solutions. These pyrosulfites (metabisulfites) are nonhygroscopic and more stable than the corresponding sulfites and bisulfites.

The alkali metal sulfites and bisulfites exist in the solid state as well as in solution. Sulfites of many of the other metals exist in the solid state and are sparingly soluble,

while their more soluble bisulfites exist only in solution. Sulfites form complexes with many of the heavy-metal salts, the sulfite radical occupying one or more of the available coordination positions. Aqueous solutions of formaldehyde react with sodium bisulfite to form sodium formaldehyde bisulfite (see *Formaldehyde*, Vol. 6, p. 865).

Many of the uses of sulfur dioxide depend on the fact that sulfurous acid and its salts are excellent low-cost reducing agents. Oxidation to sulfate is rapid and quantitative with halogens. The action with oxygen is slow and is accelerated in the presence of certain reducing agents such as ferrous or arsenite ions, while many organic substances and stannous chloride inhibit the action. Many common oxidizing agents, such as peroxide, permanganate, ferric ion, and manganese dioxide, lead to the formation of dithionate,  $\text{S}_2\text{O}_6^{2-}$  as well as sulfate. In acid solutions, sulfurous acid will act as an oxidizing agent in the presence of many reducing agents such as hydrogen sulfide, hydrogen iodide, reduced metal salts, and zinc. The reactions are complex. Sulfur is usually stated to be a product of these reductions although there is reason to believe that higher polythionic acids are actually formed. Depending on the reducing agents used, hydrogen sulfides, hydrogen polysulfides, dithionic acid, sulfate, and thio-sulfate may also be formed, indicating simultaneous oxidation and reduction of sulfurous acid in some cases (37).

#### ANALYSIS

The most common methods of analysis of sulfur dioxide in various materials are based on its reducing action in aqueous solution either as sulfurous acid or in the form of bisulfites, sulfites, and other related compounds. Titration with iodine,  $\text{SO}_2 + \text{I}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{SO}_4 + 2 \text{HI}$ , is most frequently employed, although other oxidizing agents are used in some methods. A common method is to add a fixed amount of standard iodine and then titrate the excess iodine with standard sodium thiosulfate and a starch indicator. Where colored solutions are involved or certain interfering substances are present, distillation methods are employed. The most widely used method of this type is the A.O.A.C. version of the Monier-Williams procedure (1). This method involves distilling sulfur dioxide into hydrogen peroxide and titrating the sulfuric acid formed with standard alkali using bromophenol blue as indicator. Sulfur dioxide in gas mixtures can be determined by bubbling the gas through standard iodine solution to point of discharge of the iodine-starch color. Sulfurous acid and bisulfites may also be determined by titration as acids with standard alkali solution.

#### MANUFACTURE

In most chemical process applications requiring sulfur dioxide gas or sulfurous acid, sulfur dioxide is prepared by the burning in air of sulfur or pyrite,  $\text{FeS}_2$ , usually the former. A large number of sulfur and pyrites burners have been developed for the sulfuric acid (*q.v.*) and wood pulp (see *Pulp*) industries (14,32), which produce and immediately consume about 97% of some 9 million tons of captive sulfur dioxide annually in the U.S.

The production of sulfur dioxide gas by the combustion of Frasch process sulfur is relatively simple and is the preferred method, except in cases in which economic considerations favor the use of pyrite. For most applications, with the exception of sulfuric acid manufacture, as high a sulfur dioxide content as possible is desired. For sulfur burners the theoretical maximum is 21%  $\text{SO}_2$  by volume, and under satis-

factory conditions from 14% to as high as 20% may be achieved. The various sulfur burners commercially available are rated by their manufacturers as capable of producing gas in the range of from 5 to 18% sulfur dioxide. In the upper range of sulfur dioxide concentration, theoretical flame temperatures for the combustion of sulfur in air range from 1200 to 1600°C. The temperature of gas leaving the combustion chamber in continuous sulfur burners ranges from 700 to 1000°C. One pound of sulfur requires one pound of oxygen for its complete combustion. This is the amount contained in 53.8 cu.ft. of air. The reaction produces 1942 B.t.u./lb. of sulfur dioxide produced (from rhombic sulfur at 25°C.).

Most sulfur burners in use today are of two types: rotary burners and spray burners. These have replaced the earlier pan or retort type. The latter suffered mainly from irregular gas strength and temperatures, along with higher losses and difficulty in handling the organic scum formed on the burning surfaces. Best known and most widely used of the modern rotary burners is the Glens Falls Rotary Sulfur Burner manufactured by Glens Falls Machine Works. The burner consists of a horizontal steel cylinder that slowly rotates to keep the interior surfaces wet with molten sulfur, which is maintained at close to overflow level either by mechanical solid feed or preferably by liquid feed from an external sulfur melter. Air is drawn through the burner by a draft of from 0.25 to 2 in. applied to the discharge end. At all but the lowest drafts and capacities, the cylinder is followed by a brick-lined after-burner or combustion chamber into which further air may be admitted through dampers. Rated capacities range from 5 to 2000 lb. of sulfur per hour. Several improvements have been proposed in the rotary burner to permit use of sulfurs of high bituminous content (25). These include tilting of the burner cylinder for continuous overflow of carbonaceous scum into the combustion chamber, fins within the burner to increase surface and insulation to increase temperature for increased capacity, and better ashing of bituminous matter. Regulation of the air supply is the most important factor in the burning of sulfur to form sulfur dioxide. Excess air, particularly if it is moist and if operating temperatures are too low, will lead to formation of sulfur trioxide and about 2 or 3% of sulfur is usually lost in this way. A lesser difficulty is the formation of sublimed sulfur as a result of overheating the burner (25) or if too little air is used once the burner has come to temperature. A properly operated after-burner can practically eliminate this source of loss.

Several other types of sulfur burners are available to meet various needs, each offering particular advantages of its own. A compact type of rotary sulfur burner is made by American Paper Machinery and Engineering Co. with rated capacities from 10 to 833 lb. of sulfur per hour. A nonrotary type of continuous sulfur burner with capacities from 25 to 1350 lb. per hour, offered by Acme Coppersmithing and Machine Co., can operate either under pressure or under vacuum. A successful sulfur spray burner that is particularly suitable when high capacities are needed has been offered by Chemical Construction Corporation in recent years. Molten sulfur is pumped through a spray gun into a brick-lined combustion chamber. Air is supplied under pressure by a blower. A waste heat boiler utilizes the heat of combustion to make steam for melting and pumping the sulfur. Capacities range from 250 to 14,000 lb. of sulfur per hour. Quick starting and stopping and ease of regulation are among the advantages claimed for spray burners.

The burning of pyrite is considerably more difficult to control than the burning of sulfur, although many of the difficulties have been overcome in modern mechanical

pyrite burners, of which the Herreshoff and Wedge burners are well-known types (see also *Sulfuric acid*). The pyrite is burned on multiple trays which are subject to mechanical raking. The theoretical maximum  $\text{SO}_2$  content is 16.2% and levels of 10–14% are generally attained. As much as 13% of the sulfur in pyrite may be converted to sulfur trioxide in pyrite burners. The spent pyrite may contain up to 4% of sulfur. In most applications the separation of dust is necessary when sulfur dioxide is made from pyrite. Several methods may be employed for this (see *Gas purification*), but for many purposes the use of water spray towers is most satisfactory. This also serves to remove some of the sulfur trioxide and to cool the gas. For most applications burner gases need no further treatment other than cooling to permit their absorption either by water or by alkaline solutions or slurries. Lead pipes in flowing water are generally used, about 15 sq.ft. of cooling surface per ton per day of  $\text{SO}_2$  being sufficient to cool the gas to near ambient temperatures.

There are about ten manufacturers of *liquid sulfur dioxide* in the U.S. and Canada at the present time. Sulfur dioxide is obtained from one of two sources—from the burning of sulfur and from waste gases, usually smelter gases, although at least one manufacturer uses waste from phenol production. Most plants in the U.S. utilize sulfur as their starting material and employ water as the absorbent in various modifications of the old Hönisch-Schröder process (20) first described in 1884. The cooled sulfur burner gas is blown into the bottom of packed towers down which water flows. The exit gas contains from 0.02–0.1% sulfur dioxide while the rich absorbent contains 1–2% of  $\text{SO}_2$ . The cool rich liquor is stripped by heating with low pressure steam. The stripped liquor contains about 0.01%  $\text{SO}_2$  and is discharged. The gaseous mixture of sulfur dioxide and water vapor leaving the stripper is then dried with sulfuric acid and finally compressed and liquefied. From 50 to 100 tons of water is required per ton of sulfur dioxide produced. Because of the large volume of water required and the heavy heat losses in stripping this process is relatively expensive and unsuited for the recovery of sulfur dioxide from waste gases.

At least two plants in the United States manufacture liquid sulfur dioxide from lead and copper smelter gases at about 5% strength by a process based on absorption in dimethylaniline (18). This process has important advantages over other alkaline absorption methods, principally because of its economies in materials, space, and equipment. Losses due to oxidation of sulfite to sulfate are also minimized. The flue gas containing sulfur dioxide coming from the smelter is first cleaned by passage in turn through a hot Cottrell precipitator for removal of dust and fumes, a water scrubber for removal of residual fume and for cooling and conditioning the gas, a Cottrell mist precipitator for removing water droplets and sulfuric acid mist, and finally a coke filter to remove the last trace of water droplets. The clean gas is then cooled and passed through a bubble-cap tower, where it is absorbed in cool anhydrous dimethylaniline. The tail gas which is vented to the atmosphere contains about 0.05%  $\text{SO}_2$ . The rich absorbent is passed through a heat exchanger to a second bubble-cap tower, where it is stripped with steam. The mixture of sulfur dioxide and water vapor is cooled and scrubbed with water to remove any residual dimethylaniline. The purified gas is dried with sulfuric acid and is then compressed, cooled, and liquefied to the final product containing less than 50 p.p.m. of water. Efficient recovery of the absorbent from both gas and liquid phases is an important feature of the process, and the consumption of dimethylaniline is only about 1 lb. per ton of sulfur dioxide produced.

Many other alkaline absorbents have been utilized or studied for the recovery

of sulfur dioxide from dilute gases (23). These include ammonia, basic aluminum sulfate, and various aromatic and aliphatic amines. At Copper Cliff, Ontario, liquid sulfur dioxide is produced by direct compression without the use of an absorption process from nickel smelter gases. This is made possible by a sulfur dioxide content on the order of 75% in the gases resulting from a flash roasting process using pure oxygen instead of air (38).

#### MATERIALS OF CONSTRUCTION (26)

Almost all common materials of construction are resistant to commercial dry liquid sulfur dioxide, dry sulfur dioxide gas and hot sulfur dioxide gas containing water above the dew point. These include cast iron, carbon steel, copper, brass, and aluminum. Where hot gases or hot solutions are involved, the temperature resistance, particularly for plastics and resins, and the resistance to thermal shock, particularly for ceramic, glass and stone, should be taken into account. The latter materials are inert to the wet gas, sulfurous acid, and sulfite solutions. Carbon, graphite, and impregnated carbon are suitable for practically all types of sulfur dioxide service. Lead is also resistant to sulfur dioxide and sulfites under most conditions except those ruled out by its mechanical and physical limitations. Aluminum is resistant under a variety of conditions, and is favored in some food industry applications involving wet sulfur dioxide. Organic coatings are generally resistant, but may fail where gas diffusion through the film is appreciable. Among the organic materials, hard rubber has been found satisfactory in sulfurous acid at moderate temperatures and butyl rubber may be expected to perform similarly.

Iron, steel, Monel, nickel and Inconel are common materials satisfactory for dry or hot sulfur dioxide but they are readily corroded below the dew point or by wet sulfur dioxide gas, sulfurous acid, and sulfites. Inconel is especially resistant to very hot sulfur dioxide gas. Metals best suited to a wide variety of wet, dry, and hot sulfur dioxide, sulfurous acid, and sulfite service are Worthite, Durimet 20, and several of the stainless steels. Liquid sulfur dioxide will discolor iron, copper, and brass at about 300 p.p.m. of moisture, and will produce light scale at about 0.1% moisture and serious corrosion at about 0.2% or higher moisture content. Copper and brass can be used in a wide variety of light sulfur dioxide wet service. Wooden tanks are widely used for sulfurous acid preparation, handling, and storage. Sulfite pulp digestors are made of steel lined with acid-resisting brick. Thermosetting phenolic and furan resins and various inorganic acid resistant cements have been used for digester mortar joints resistant to the hot bisulfite liquors.

#### GRADES AND SPECIFICATIONS

The major grade of liquid sulfur dioxide sold is variously known as the technical, industrial, or commercial grade. This grade contains a minimum of 99.98% of sulfur dioxide and is a water-white liquid free of sulfur trioxide and sulfuric acid and showing only a trace at most of nonvolatile residue. Its most important specification is the moisture content, which is generally set at 100 p.p.m. maximum. The only other grade sold is the refrigeration grade of liquid sulfur dioxide, which is a premium grade having the same purity and specifications as the industrial grade except for the moisture content, specified as 50 p.p.m. maximum (8). At least one manufacturer sells a single grade for which specifications have been established as follows: color, APHA 25 max.; nonvolatile residue, 25 p.p.m. max.; moisture, 50 p.p.m. max.

## SHIPPING, STORAGE, AND HANDLING

Liquid sulfur dioxide is shipped in tank cars, ton drums, and cylinders. All shipping containers are governed by regulations of the Interstate Commerce Commission (6), which classifies sulfur dioxide as a nonflammable compressed gas. The various containers are made of specified steel, must pass hydrostatic pressure tests, and are protected by safety devices. Single unit tank cars are available in 32,000, 40,000, or 60,000 lb. capacities. Sulfur dioxide tank cars are lagged and provided with a spring-loaded pressure relief valve. Purchasers of tank car quantities of sulfur dioxide are required to have adequate storage facilities for prompt transfer from tank cars.

Ton drums containing 2000 lb. of sulfur dioxide are shipped on multiunit railroad cars holding 15 drums. These drums are provided with fusible safety plugs which melt at 165°F. Since purchaser ordinarily retains the drums until empty, they serve as their own storage containers. The common cylinder size for sulfur dioxide is the 150 lb. container, although other cylinder sizes are available for refrigeration grade material. Cylinders are also provided with 165°F. fusible safety plugs and carry the green label for nonflammable gases.

All shipping containers for liquid sulfur dioxide are arranged so that withdrawal or transfer of the contents may be effected either as a gas or as a liquid. In general the pressure of the sulfur dioxide itself in its container is utilized to effect the transfer. The most convenient method of attaining the required pressure differential in the case of cylinders and drums is heating. Since these containers are equipped with fusible plugs it is recommended that the temperature never be allowed to exceed 125°F. either in storage or during heating for transfer (8). In order to minimize the danger that a container of sulfur dioxide will become full of liquid and fail due to the development of hydrostatic pressure with rising temperature, the maximum allowable sulfur dioxide capacity, in pounds, of any container has been set by the I.C.C. at 1.25 times the water capacity, in pounds. To allow for safety under all possible conditions it is common practice to fill containers to only 1.15 times the water capacity.

## HEALTH AND SAFETY FACTORS

Sulfur dioxide presents two potential hazards: one is its physiological action as an irritating, asphyxiant gas; the other is its freezing action when in contact with the skin or other tissues in the form of a liquefied low-boiling gas. Cases of severe exposure to sulfur dioxide gas are rare because the gas is so strongly irritating that it serves as its own warning agent at very low concentrations. Exposure to high concentrations for even short periods may be dangerous in that suffocation may result from involuntary shutting of the glottis to keep out the gas. Fortunately the irritation caused by sulfur dioxide is so severe that a person will not remain in a contaminated atmosphere unless trapped. There is no evidence that continued exposure to sulfur dioxide in allowable concentrations produces a cumulative effect.

The physiological response to various concentrations of sulfur dioxide gas are shown in Table XII, assembled from various sources (8).

Green plant life is far more sensitive to sulfur dioxide gas than are man and animals. Injury to vegetation may occur at ground level concentrations under 1 p.p.m. The damaging effects of sulfur dioxide on plants and animals particularly in the vicinity of smelters and other industrial process and power plants has led to regulations designed to limit the amount of atmospheric contamination in many countries, cities,



TABLE XII. Physiological Response to Sulfur Dioxide Gas.

	p.p.m.
Least detectable odor.....	3 to 5
Least amount causing immediate eye irritation.....	20
Least amount causing immediate throat irritation.....	8 to 12
Least amount causing coughing.....	20
Max. concn. allowable for prolonged exposure.....	10
Max. concn. allowable for short ( $\frac{1}{2}$ hr.) exposure.....	50 to 100
Dangerous for even short exposure.....	400 to 500

and areas of the world (23). The increasing necessity of limiting atmospheric pollution by sulfur dioxide and other sulfur compounds has been one of the important factors in the recent growing practice of removing sulfur compounds from waste process gases and recovering their sulfur values in many cases.

Sulfur dioxide does not form explosive or combustible mixtures with air and does not offer any fire hazards. A Chemical Safety Data Sheet, Manual Sheet SD-52, on Sulfur Dioxide, adopted July 1953, is available from Manufacturing Chemists' Association, Inc., Washington, D.C.

#### ECONOMIC ASPECTS

The growth of anhydrous liquid sulfur dioxide over the past 15 years is indicated in Table XIII, assembled from various government sources (34).

TABLE XIII. Production, Shipments, and Prices of Liquid Sulfur Dioxide.

Year	Production, short tons	Consumed by producing plants, short tons	Shipments, <sup>a</sup> short tons	Price, \$/lb. c.i., tks., f.o.b. wks.
1939	Not avail.	Not avail.	13,486	—
1942	28,335	Not avail.	Not avail.	0.040
1947	44,869	Not avail.	27,207	0.044
1950	43,564	11,756	31,411	0.045
1951	52,662	13,953	39,100	0.045
1952	43,755 <sup>b</sup>	Not avail.	Not avail.	0.045

<sup>a</sup> Sales and interplant transfers.

<sup>b</sup> Preliminary.

Annually in the U.S., about 8 million tons of sulfur dioxide is converted into sulfuric acid, at least another million tons is produced for various captive uses (mainly the production of sulfite pulp), and about 40,000 tons is turned out as commercial liquid sulfur dioxide, for miscellaneous noncaptive uses.

In single 150 lb. cylinders, liquid sulfur dioxide costs 12 cents per pound as against 5.35 cents in carload drums and 4.5 cents in single unit tank cars.

#### USES

Aside from the enormous consumption of sulfur dioxide in the manufacture of sulfuric acid and sulfite pulp, approximately 270,000 tons of sulfur dioxide is consumed each year in a wide variety of industrial and agricultural applications. The uses for sulfur dioxide stem from its several aspects as a reducing agent (bleach, antichlor), a preservative and fumigant, a liquid solvent (extractant), an easily compressible condensable gas (refrigerant), a stable gas (inert atmosphere), and a low-cost reagent for

the manufacture of chemicals (36). Many of the important applications of sulfur dioxide are to be found in the food industries and in the related fields of agricultural, animal, and vegetable products, where one or more of its functions as a fumigant, preservative, and bleach are utilized. (See Vol. 6, p. 837.) Certain fruits, such as grapes, that are subject to rapid spoilage can more safely be shipped and stored prior to processing if fumigated with sulfur dioxide. Stored grains and cereals are fumigated with sulfur dioxide to overcome infestation by insects and rodents. In the manufacture of wine a small amount of sulfur dioxide is added to the must to destroy bacteria, molds, and wild yeasts without harming the yeasts that produce the desired fermentation. Sulfur dioxide is used as a bleaching agent in the refining of sugar and in the processing of fruits and grains and to prevent browning of apple slices. It is also useful as a preservative in the sun-drying and artificial drying of various fruits. Sulfur dioxide is also used as a preservative and bleach in the brining of cherries. It is widely used as an extractant, precipitant, bleach, and preservative in the manufacture of various industrial and food proteins such as soybean protein, casein, gelatin, and glue. Of some interest also is its use as a silage preservative.

Many uses have been proposed for liquid sulfur dioxide as a reaction medium and an extractant. These include Friedel-Crafts condensations, isomerization, and sulfonation reactions. Among various extraction processes, one—the Edeleanu petroleum refining process—has found commercial application (see Vol. 10, p. 149). It is based on the fact that aromatics, unsaturates, and sulfur compounds are readily miscible with it while saturated hydrocarbons have only limited solubility.

Sulfur dioxide finds many uses as a raw material in the manufacture of chemicals. Its uses in the manufacture of sulfites, bisulfites, metabisulfites, and hydrosulfites are well known. Liquid sulfur dioxide has been used in the manufacture of sulfuryl and thionyl chlorides and a variety of organic sulfonates, sulfones, and sulfonyl chlorides. In recent years the reactions of sulfur dioxide with anthracite to produce carbon disulfide (31) and with olefins to produce thiophene (9) have been studied.

Miscellaneous uses for sulfur dioxide include adjustment of chlorine in water supplies, treatment of boiler waters, bleaching of various fiber and mineral products, cleaning of filter beds and wells, as an inert atmosphere in magnesium metallurgy, as a surface alkali neutralizer in glass manufacture, preparation of chrome liquor for leather tanning, as a refrigerant in mechanical refrigerators, as an antichlor in textile processing, in ore flotation, and many other minor uses.

### Sulfur Oxygen Acids and Their Salts.

**Dithionic acid.** See *Thionic acids*.

**Dithionous acid** (hydrosulfurous acid). This acid,  $\text{H}_2\text{S}_2\text{O}_4$ , is formed by passing aqueous sulfurous acid through a column containing amalgamated zinc granules (Jones reductor). The acid is very unstable and breaks down rapidly into thiosulfate, bisulfate, or, if the reaction medium is sufficiently acid, into sulfurous acid and sulfur. The free acid has never been isolated, but its salts, particularly the sodium and zinc salts, have been prepared and are well known articles of commerce. The salts were originally termed hydrosulfites as a consequence of the composition first assigned to them following their initial preparation in 1869; this designation has persisted to the present day as the exclusive commercial name. After the present formula was established, the names hyposulfurous acid and hyposulfites were widely used in the litera-

ture. In more recent years the names dithionous acid and dithionites have been proposed and widely adopted in the literature to avoid confusion with the "hypo" of commerce, which is sodium thiosulfate.

*Sodium dithionite (hydrosulfite)*,  $\text{Na}_2\text{S}_2\text{O}_4$ , crystallizes from solution as a dihydrate that oxidizes rapidly in air to sodium metabisulfite. The anhydrous salt is much more stable and is the form more commonly manufactured. In the ten years from 1941 to 1951, production of this salt has increased from about 16,000 to about 30,000 short tons (100% basis) per year (34). The commercial material is marketed as a dry white crystalline powder of about 94% purity. Some large textile users manufacture the salt at their own plants in the form of solutions. *Zinc hydrosulfite* is also produced commercially to the extent of perhaps 1000 tons per year and is marketed as a fine white powder containing about 80% of zinc dithionite. Zinc hydrosulfite is less active and more stable, at a given temperature and pH, than is sodium hydrosulfite; hence it is used only in applications requiring higher temperatures or lower pH than for the latter.

Dithionites are prepared by the reduction of sulfites, bisulfites, and sulfur dioxide with reductants such as iron or zinc powder, sodium or zinc amalgam, or sodium suspension. The electrolytic reduction of sodium bisulfite to sodium dithionite in a hydrogen atmosphere has also been studied (27). Although few particulars are available on the methods of manufacturing hydrosulfites in the U.S., considerable information on German practice has been made available since the close of World War II. One process that has been described in detail (12) involves as a first step the reduction of liquid sulfur dioxide in a continuous reactor with zinc dust slurried in water. The reaction mixture is circulated through a tubular cooler at 35°C. and zinc hydrosulfite is continually bled off. The filtered liquor is converted in a large vessel to the sodium salt by means of 25° caustic soda. The resultant slurry of zinc hydroxide and sodium hydrosulfite is filtered and washed several times after being treated with sodium sulfide to remove heavy metals. The ensuing 20% solution is then salted out with the aid of salt and alcohol. The resulting crystals are partially decanted and dehydrated by means of direct steam at about 65°C., and after further removal of mother liquor the crystals are washed with alcohol and finally vacuum-dried at 80 to 90°C. Almost all of the equipment involved is stainless steel or is rubber-covered or enameled. Solutions of zinc or sodium hydrosulfite can be economically manufactured on location by large users by methods that have been developed over a number of years by Virginia Smelting Company, using liquid sulfur dioxide. One simple method produces 3 lb. of zinc hydrosulfite per gallon of solution by the introduction of liquid sulfur dioxide into a well-agitated, water-cooled tank containing a water suspension of zinc dust.

The commercial utilization of the dithionites is based on their powerful reducing action on many materials. They readily reduce a large number of metal ions to the metal, reduce disulfide linkages in wool and hair, and reduce a large number of nitro compounds and many dyes. Principal applications are in various textile operations (5) such as dyeing, printing, and stripping. Other important uses include bleaching of groundwood pulp, soap, sugar, molasses, and glue.

**Hydrosulfites.** See p. 426.

**Metabisulfites.** See "Pyrosulfurous acid," p. 428.

**Peroxsulfuric acids, Persulfuric acids.** See Vol. 10, pp. 45-48.

**Polythionic acids.** See *Thionic acids*.

**Pyrosulfuric acid.** Sulfur trioxide forms a hydrate (among several others) with water which corresponds to the composition  $\text{H}_2\text{S}_2\text{O}_7$ , or pyrosulfuric acid, melting at  $36^\circ\text{C}$ . The acid is very unstable and upon dissolving in water or on heating it behaves like a mixture of sulfuric acid and sulfur trioxide. A series of pyrosulfates exists, the best known of which are the alkali metal pyrosulfates, formed by strongly heating the appropriate bisulfate. Although these salts give definite x-ray diffraction patterns and contain a definite  $\text{S}-\text{O}-\text{S}$  linkage, they hydrolyze readily in water to yield bisulfate and sulfate ions. The alkali metal pyrosulfates melt more readily than the corresponding sulfates and give up sulfur trioxide upon calcining, to form the sulfate. Trisulfates,  $\text{M}_2\text{S}_3\text{O}_{10}$ , having similar structures and properties to the pyrosulfates are known. They are formed by reacting the alkali metal sulfate with excess sulfur trioxide. The trisulfates hydrolyze readily in water to yield bisulfates (30).

**Pyrosulfurous acid,**  $\text{H}_2\text{S}_2\text{O}_5$ , is known only through its salts, the pyrosulfites or, as they are known commercially, the metabisulfites,  $\text{M}_2\text{S}_2\text{O}_5$ , formed by the heating of alkali metal bisulfites. The uses of the metabisulfites are similar to those of the bisulfites, with which they are closely associated. Most of the sodium bisulfite sold commercially is in the form of its anhydride, sodium metabisulfite, since the latter is less hygroscopic and more stable in storage and shipment. The production of sodium bisulfite and metabisulfite from 1941 to 1945 in the United States was about 20,000 tons per year.

**Sulfoxylic acid.** Free sulfoxylic acid,  $\text{H}_2\text{SO}_2$ , is unknown. Reports of its sodium and zinc salts may be due to an analytical error. The structure  $\text{S}(\text{OH})_2$ , sulfur (II) hydroxide, is known only as esters,  $\text{ROSOR}$ , and amides,  $\text{R}_2\text{NSNR}_2$ . Derivatives of a sulfinic acid form,  $\text{HSO}_2\text{H}$ , for example ester salts,  $\text{HOCH}_2\text{SO}_2\text{M}$ , and a cobalt complex,  $(\text{Co}(\text{SO}_2))_x$  are known. See also *Sulfinic acids*, p. 311.

The ester salts are prepared (5,12) by the addition of formaldehyde to the appropriate dithionite salt and have the structure exemplified by sodium formaldehydesulfoxylate,  $\text{NaSO}_2\text{CH}_2\text{OH}$ . Three commercial salts are produced, amounting to a total of about 6500 tons in 1951 in the U.S. These are the sodium salt in the form of a white granular dihydrate of about 100% purity, a normal zinc salt,  $\text{Zn}(\text{SO}_2\text{CH}_2\text{OH})_2$ , which is a white crystalline powder of at least 95% purity, and a basic zinc salt,  $\text{Zn}(\text{OH})\text{SO}_2\text{CH}_2\text{OH}$ , which is a light gray powder of about 89% purity. The formaldehydesulfoxylates find in general the same applications as the hydrosulfites (dithionites) except that they are somewhat less active and more stable. They are therefore used in many bleaching and reducing applications at higher temperatures and lower pH values than the corresponding hydrosulfites. The sulfoxylates are best applied at a pH of about 3.4 as against an optimum pH of about 6 for zinc hydrosulfite and about 9.5 for sodium hydrosulfite. The basic zinc formaldehydesulfoxylate is the most stable of the series and can be used at temperatures around  $100^\circ\text{C}$ . as against a preferred temperature of about  $50^\circ\text{C}$ . for sodium hydrosulfite. An important application of sodium formaldehydesulfoxylate is to directly introduce the group,  $-\text{CH}_2\text{SO}_2\text{Na}$ , upon nitrogen as in the preparation of the medicinal neoarsphenamine (see Vol. 2, p. 126). The principal function of the sulfuate group in this and related cases is to increase the water solubility of the compound; it is readily split off *in vivo*. The sulfoxylates have been marketed under a number of trade names, Formopon, Rongalite, Dekrolin, and Sulfoxite being among the better known ones.

**Sulfuric acid** (*q.v.*).

**Sulfurous acid.** See "Sulfur dioxide," p. 419.

**Thiocarbamic acids; Thiocarbonic acids; Thioformic acid.** See *Thio acids*.

**Thiophosphoric acids.** See Vol. 10, p. 493.

**Thiosulfuric acid and thiosulfates** (*q.v.*).

### Bibliography

- (1) A.O.A.C. *Method of Analysis*, 7th ed., Washington, D.C., 1950.
- (2) Barrow, G. M., and Pitzer, K. S., *Ind. Eng. Chem.*, **41**, 2737 (1949).
- (3) Bice, W. O., Prange, F., and Weis, R. E., *Ind. Eng. Chem.*, **44**, 2497 (1952).
- (4) Bottoms, R. R., *Ind. Eng. Chem.*, **23**, 501 (1931).
- (5) Brearley, G., and Starkie, J., *J. Soc. Dyers Colourists*, **64**, 278 (1948).
- (6) Campbell's Freight Tariff #4 and Motor Carrier Tariff #7, Association of American Railroads, Bureau of Explosives, 30 Vesey St., New York 7, N.Y.
- (7) *Chemical Abstracts*, **46**, 7451c (1952); **47**, 2076d, 5838e (1953).
- (8) Compressed Gas Association, Inc., New York, N.Y., *Sulfur Dioxide*, Pamphlet G-3, Adopted 1949.
- (9) Conary, R. F., et al., *Ind. Eng. Chem.*, **42**, 467 (1950).
- (10) Cunningham, W. A., *Ind. Eng. Chem.*, **42**, 2238 (1950).
- (11) Dryden, I. G. C., *J. Soc. Chem. Ind. London*, **66**, 59 (1947).
- (12) Edwards, W. A. M., and Clayton, J. H., *Sodium Hydrosulfite and Related Compounds, I. G. Ludwigshafen*, BIOS Repts. 422 (PB 34027) and 271 (PB 22409); U.S. Dept. of Commerce, Office of Technical Services.
- (13) Espach, R. H., *Ind. Eng. Chem.*, **42**, 2235 (1950).
- (14) Fairlie, A. M., *Sulfuric Acid Manufacture*, Reinhold, N.Y., 1936.
- (15) Fanelli, R., *Ind. Eng. Chem.*, **41**, 2031 (1949).
- (16) Feher, F., and Baudler, M., *Z. anorg. Chem.*, **253**, 170 (1947).
- (17) Feher, F., and Baudler, M., *Z. anorg. Chem.*, **258**, 132 (1949).
- (18) Fleming, E. P., and Fitt, T. C., *Ind. Eng. Chem.*, **42**, 2253 (1950).
- (19) Freitag, R., *Zucker*, **3**, 16 (1950).
- (20) Hitchcock, L. B., and Scribner, A. K., *Ind. Eng. Chem.*, **23**, 743 (1931).
- (21) Jander, G., and Wickert, K., *Z. physik. Chem.*, **178**, 57 (1936).
- (22) Katz, M., *Ind. Eng. Chem.*, **41**, 2450 (1949).
- (23) Katz, M., and Cole, R. J., *Ind. Eng. Chem.*, **42**, 2258 (1950).
- (24) Kelley, K. K., *Contributions to the Data on Theoretical Metallurgy. VII. The Thermodynamic Properties of Sulfur and Its Inorganic Compounds*, Bulletin 406, U.S. Dept. of the Interior, Bureau of Mines, 1936, pp. 18-24.
- (25) Lippman, A., Jr., *Ind. Eng. Chem.*, **42**, 2215 (1950).
- (26) Materials of Construction Report (14th), *Chem. Eng.*, **57**, 136 (1950).
- (27) Patel, C. C., and Rao, M. R. A., *Proc. Natl. Inst. Sci. India*, **15**, 131 (1949).
- (28) Riesenfeld, F. C., and Blohm, C. L., *Petroleum Refiner*, **29**, No. 4, 141 (1950).
- (29) Rorschach, R. L., and Gardner, F. T., *Ind. Eng. Chem.*, **41**, 1380 (1949).
- (29a) Schenk, P. W., *Ber.*, **75**, 94 (1942).
- (30) Sidgwick, N. V., *Chemical Elements and Their Compounds*, 1950, Vol. II.
- (31) Siller, C. W., *Ind. Eng. Chem.*, **40**, 1227 (1948).
- (31a) Spandau, H., and Brunneck, E., *Z. anorg. u. allgem. Chem.*, **270**, 201 (1952).
- (32) Sutermeister, E., *Chemistry of Pulp and Paper Making*, 3rd ed., Wiley, N.Y., 1948.
- (33) Thorne, P. C. L., and Roberts, E. R., *Ephraim's Inorganic Chemistry*, 4th ed., revised, Nordeman, N.Y., 1943.
- (34) U.S. Dept. of Commerce, Bureau of Census, *Parts for Industry, Series M19A*.
- (35) West, J. R., *Chem. Eng. Progr.*, **44**, 287 (1948).
- (36) Willson, C. S., et al., *Chem. Inds.*, **53**, 178 (1943).
- (37) Yost, D. M., and Russell, H., *Systematic Inorganic Chemistry*, Prentice-Hall, N.Y., 1944.
- (38) Zabel, H. W., *Chem. Inds.*, **63**, 960 (1948).
- (39) Brit. Pat. 633,469 (March 18, 1950), R. Darlington, V. Oakes, and K. C. Roberts (to Anchor Chemical Co., Ltd.).

- (40) U.S. Pat. 2,362,057 (Nov. 7, 1944), J. P. Edwards (to Hooker Electrochemical Co.).  
 (41) U.S. Pat. 2,420,623 (May 13, 1947), W. H. Salzenberg and M. Sveda (to Du Pont).  
 (42) U.S. Pat. 2,431,823 (Dec. 2, 1947), A. Pechukas (to Pittsburgh Plate Glass Co.).  
 (43) U.S. Pat. 2,471,946 (May 31, 1949), E. F. Fricke (to Allied Chemical & Dye Corp.).  
 (44) U.S. Pat. 2,530,410 (Nov. 21, 1950), M. Sveda (to Du Pont).

ALVIN SCHALLIS AND PAT MACALUSO

## SULFUR COMPOUNDS, ORGANIC

A large variety of organic sulfur compounds is possible because of the ability of the sulfur atom to exhibit many valence states. Sulfur compounds having bivalent, tetravalent, and hexavalent sulfur are known. Organic sulfur compounds are often compared with oxygen compounds, but this can be very misleading (7,8). Some of the major differences result from: the ability of sulfur to unite with itself to form chains giving di-, tri, tetra-, and polysulfides; the lower capacity of sulfur to hold hydrogen and the greater capacity to unite with negative elements; and the ability of sulfur to

TABLE I. Classes of Organic Sulfur Compounds.

Structural formula	Name	Remarks
I. Compounds of C, H, and S.		
$R-SH$	Mercaptans, thiols	Thioalcohols and thiophenols (when R is aromatic).
$R-S-R$	Sulfides, thioethers	
$\begin{array}{c} \diagup \quad \diagdown \\ S \\ \diagdown \quad \diagup \\ (CH_2)_x \end{array}$	Cyclic sulfides	Thiophanes or tetrahydrothiophenes (5-membered ring).
$R-S-S-R$	Disulfides	
$R-S_x-R$	Polysulfides	Trisulfides probably linear; higher sulfides may branch or cyclize.
$\begin{array}{c} S \\ \diagup \quad \diagdown \\ HC \quad CH \\ \diagdown \quad \diagup \\ HC \quad CH \end{array}$	Thiophene, thiofuran	
$\begin{array}{c} S \\    \\ R-C-SH \end{array}$	Dithio acids	Unstable, but derivatives may be formed.
$\begin{array}{c} S \\    \\ R-C-H \end{array}$	Thioaldehydes, thials	More commonly exist as cyclic trimers.
$\begin{array}{c} S \\    \\ R-C-R \end{array}$	Thioketones, thiones	More commonly exist as cyclic trimers.
$\begin{array}{c} H \quad SR \\ \diagdown \quad \diagup \\ C \\ \diagup \quad \diagdown \\ R \quad SR \end{array}$	Mercaptals, thioacetals	
$\begin{array}{c} R \quad SR \\ \diagdown \quad \diagup \\ C \\ \diagup \quad \diagdown \\ R \quad SR \end{array}$	Mercaptals, mercaptoles	

TABLE I. Classes of Organic Sulfur Compounds (*Concluded*).

Structural formula	Name	Remarks
II. Neutral compounds of C, H, S, and O.		
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{R}-\text{S}-\text{R} \end{array}$	Sulfoxides	Unsymmetrical compounds, optically active.
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{R}-\text{S}-\text{R} \\ \downarrow \\ \text{O} \end{array}$	Sulfones	
III. Acid compounds of C, H, S, and O.		
$\text{R}-\text{S}-\text{OH}$	Sulfenic acids	Only one acid known.
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{R}-\text{S}-\text{OH} \end{array}$	Sulfinic acids	Esters optically active.
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{R}-\text{S}-\text{SH} \\ \downarrow \\ \text{O} \end{array}$	Thiosulfonic acids, thiolsulfonic acids	Acids unknown, but salts and esters may be prepared.
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{R}-\text{S}-\text{OH} \\ \downarrow \\ \text{O} \end{array}$	Sulfonic acids	
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{RO}-\text{S}-\text{OH} \end{array}$	Monoesters of sulfurous acid	Diesters are (di)alkyl sulfites.
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{RO}-\text{S}-\text{OH} \\ \downarrow \\ \text{O} \end{array}$	Monoesters of sulfuric acid	Diesters are (di)alkyl sulfates.
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{RS}-\text{S}-\text{OH} \\ \downarrow \\ \text{O} \end{array}$	S-Esters of thiosulfuric acid	Esters and salts may be formed.
$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{SH} \end{array}$	Monothio acids, thiol acids	Unstable, but salts and esters may be formed.
$\begin{array}{c} \text{S} \\ \parallel \\ \text{R}-\text{C}-\text{OH} \end{array}$	Monothio acids, thiono acids	Unstable, but salts and esters may be formed.
$\begin{array}{c} \text{S} \\ \parallel \\ \text{RO}-\text{C}-\text{SH} \end{array}$	Xanthic acids	Unstable, but salts and esters may be formed.
IV. Compounds of C, H, S, and X (X = halogen).		
$\left[ \begin{array}{c} \text{R} \\   \\ \text{R}-\text{S}-\text{X} \end{array} \right]^+ \text{X}^-$	Sulfide dihalides	Hydrolyzed to sulfoxides.
$\left[ \begin{array}{c} \text{R} \\   \\ \text{R}-\text{S} \\   \\ \text{R} \end{array} \right]^+ \text{X}^-$	Sulfonium compounds, thionium compounds	Hydroxides stable; strong bases. Salts of type $[\text{RR}'\text{R}''\text{S}]^+\text{X}^-$ optically active.

unite with oxygen and the halogens to form such compounds as sulfones, sulfonyl halides, and sulfonic acids. The atomic structure which leads to these properties has been discussed under *Sulfur compounds—structure*.

In compounds of carbon, hydrogen, and sulfur, the sulfur is generally bivalent. If there is only one sulfur atom in the molecule, the two valences may be connected to one carbon atom, to two carbon atoms, or to one carbon atom and one hydrogen atom. These conditions result, respectively, in thials or thiones, sulfides, and mercaptans (thiols). The presence of more than one sulfur atom may result in a chain of sulfur atoms, as in disulfides or polysulfides, or may give more than one of the above groupings. The properties due to the sulfur atom may be changed enough by conjugation to give compounds essentially aromatic as in thiophenes. These various classes of compounds, with their structural formulas, are shown in part I of Table I.

If oxygen is also present along with the carbon, hydrogen, and sulfur, a series of neutral compounds and two series of acids may be formed. Sulfur attached to two carbon atoms (in a sulfide) may be oxidized to the sulfoxide by the addition of one oxygen atom and to the sulfone by the addition of two. One series of sulfur acids starts with the mercaptan or thiol, and by successive additions of oxygen atoms gives sulfenic acids (known chiefly through the derivatives), sulfinic acids, sulfonic acids, and sulfuric acid esters. A second series of acids based on substituting sulfur for the oxygen in carboxylic acids consists of the thiol acids: monothio (thiol and thiono) and dithio acids. The structural formulas in parts II and III of Table I are given according to one well-recognized convention. In addition to these series, one basic compound is found in the sulfonium hydroxides.

The presence of a halogen may exert a stabilizing influence on some of these compounds. The acid chlorides of the compounds in part III, Table I, are usually stable, and indeed the sulphenyl chlorides are the best argument for the existence of sulfenic acids. The addition product of a sulfide and a halogen molecule is a sulfide dihalide (Table I, part IV), which is usually postulated as an intermediate in the oxidation by halogen to the sulfoxide. The reaction of a sulfide with an alkyl halide results in a sulfonium compound; this is analogous in many respects to formation of an ammonium compound.

For the analysis of organic sulfur compounds see *Organic analysis*.

#### NOMENCLATURE

Several different systems of nomenclature have been developed for use with sulfur compounds (2,12). Much of the nomenclature results from comparison with oxygen compounds, and this has had the effect of obscuring the peculiar properties of sulfur compounds. Some of the systems used include:

(1) Radical system. Radical names have long been used with the class names mercaptan, sulfide, disulfide, sulfoxide, sulfone, sulfonate, etc., designating the sulfur-containing functional group. Thus, names such as ethyl mercaptan, diethyl sulfide, tetramethylene sulfide, ethyl sulfoxide, and ethyl sulfonate have often appeared in the literature. When a compound is symmetrical, as diethyl sulfide, the "di" is often dropped.


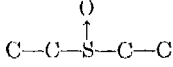
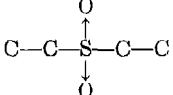
(2) Additive and substitutive system. Such terms as thiol, thio, and sulfonyl have been used to build up a name. Thus, ethanethiol, ethylthioethane (ethyl-mercaptoethane), epithiobutane, and ethylsulfonylethane are the corresponding names for the first four examples given under the radical system.



(3) "Oxa-aza-thia" or "a" system. The term "thia" has been used to designate substitution of a carbon atom and its attached hydrogen by a sulfur atom. This system usually has been reserved for cyclic sulfides or other complex compounds. However, it can be applied to simple sulfides, such as 3-thiapentane, as well as to cyclics, such as thiacyclopentane. See also *Heterocyclic compounds*.

Agreement has not been reached as to the proper place for each of the systems. The International Union of Pure and Applied Chemistry and *Chemical Abstracts* preferences are indicated in Table II, comparing nomenclature practices.

TABLE II. Nomenclature of Some Organic Sulfur Compounds.

Compound	Radical system	Additive and substitutive system	"Oxa-aza-thia" system	Miscellaneous names
$\text{C}-\text{C}-\text{SH}$	Ethyl mercaptan	Ethanethiol <sup>a,b</sup>		
$\text{C}_6\text{H}_5\text{SH}$	Phenyl mercaptan	Benzenethiol <sup>a,b</sup>		Thiophenol
$\text{C}-\text{C}-\text{S}-\text{C}-\text{C}$	Ethyl sulfide <sup>a</sup> (diethyl sulfide)	Ethylthioethane <sup>b</sup>	3-Thiapentane	
	Tetramethylene sulfide	Epithiobutane	Thiacyclopentane <sup>b</sup>	Tetrahydrothiophene <sup>a</sup>
	Ethyl sulfoxide <sup>a</sup> (diethyl sulfoxide)	Ethylsulfinylethane <sup>b</sup>	3-Thiapentane 3-oxide	
	Ethyl sulfone <sup>a</sup> (diethyl sulfone)	Ethylsulfonyl-ethane <sup>b</sup>	3-Thiapentane 3-dioxide	
$\text{C}-\text{C}-\text{S}-\text{S}-\text{C}-\text{C}$	Ethyl disulfide <sup>a</sup> (diethyl disulfide)	Ethylldithioethane <sup>b</sup>	3,4-Dithiahexane	
$\text{C}-\text{S}-\text{C}-\text{S}-\text{C}$	Dimethylmercaptal of formaldehyde	Bis(methylthio)-methane <sup>a,b</sup>	2,4-Dithiapentane	
$\text{C}-\text{S}-\text{S}-\text{S}-\text{C}$	Methyl trisulfide <sup>a</sup> (dimethyl trisulfide)		2,3,4-Trithiapentane	
$\text{C}_6\text{H}_5\text{SO}_3\text{H}$	Phenylsulfonic acid	Benzenesulfonic acid <sup>a,b</sup>		
$\text{C}_2\text{H}_5\text{SO}_2\text{Na}$	Sodium ethanesulfinate <sup>a,b</sup>			

<sup>a</sup> *Chemical Abstracts* usage.

<sup>b</sup> International Union of Pure and Applied Chemistry preference.

### Occurrence

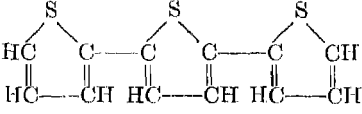
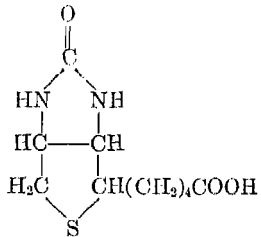
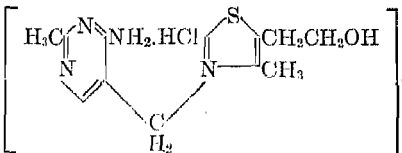
Sulfur compounds play an important part in biological processes and also are found in considerable quantity in various fuels such as coal, natural gas, shale oil, and petroleum (6). Investigation of the compounds in petroleum and natural gas (3,13) has progressed further because of the low molecular weights of some of the compounds involved.

*Sulfur Compounds in Biological Processes.* Although the presence of various sulfur compounds in natural products has been known for years, the importance of these materials to biological processes is being recognized only now (5).

Among the sulfur compound groups that have been identified are the amino acids

cystine-cysteine from keratin and glutathione, and methionine from the products of hydrolysis of wool, egg albumin, or casein. The thiol-disulfide transformation of cysteine-cystine has been indicated to be important in protein reactions. Methionine (2-amino-4-(methylthio)butyric acid) has the property of transferring methyl groups to other compounds in the growth process. Transmethylation has also been observed in the action of molds, where a disulfide is converted to an alkyl mercaptan and an

TABLE III. Occurrence of Sulfur Compounds in Biological Processes.

Compound	Structure	Isolated from
Allyl isothiocyanate	$\text{CH}_2:\text{CHCH}_2\text{NCS}$	Mustard seeds
2-Phenylethyl isothiocyanate	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{NCS}$	Nasturtium
Lanthionine	$\text{S}(\text{CH}_2\text{CH}(\text{NH}_2)\text{COOH})_2$	Wool, hair, subtilin
Cystine	$\text{S}_2(\text{CH}_2\text{CH}(\text{NH}_2)\text{COOH})_2$	Keratin (from hair, horn, etc.), glutathione (from yeast, blood, liver, etc.)
<i>p</i> -Cresolsulfuric acid	$\text{HOC}_6\text{H}_4\text{OSO}_3\text{H}$	Urine
Taurine	$\text{NH}_2\text{CH}_2\text{CH}_2\text{SO}_3\text{H}$	Bile
Alliin	$\text{CH}_2:\text{CHCH}_2\text{S}(\text{O})\text{CH}_2\text{CH}(\text{NH}_2)\text{COOH}$	Garlic
Allicin	$\text{CH}_2:\text{CHCH}_2\text{SS}(\text{O})\text{CH}_2\text{CH}:\text{CH}_2$	Garlic
Allyl sulfide	$(\text{CH}_2:\text{CHCH}_2)_2\text{S}$	Garlic
Diallyl disulfide	$(\text{CH}_2:\text{CHCH}_2)_2\text{S}_2$	Garlic
Allylthiopropene	$\text{CH}_2:\text{CHCH}_2\text{SCH}_2\text{CH}_2\text{CH}_3$	Onion
1-Propanethiol	$\text{CH}_3\text{CH}_2\text{CH}_2\text{SH}$	Onion
1-Butanethiol	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{SH}$	Skunk secretion
Bis(2-hydroxyethyl) sulfoxide	$(\text{HOCH}_2\text{CH}_2)_2\text{SO}$	Suprarenals of oxen
Sulforaphene	$\text{CH}_3\text{S}(\text{O})\text{CH}:\text{CHCH}_2\text{CH}_2\text{NCS}$	Radishes
Methyl sulfone	$(\text{CH}_3)_2\text{SO}_2$	Ox blood, plants
Methyl sulfide	$(\text{CH}_3)_2\text{S}$	Marine algae, various plants
Dimethyl-2-carboxyethylsulfonium chloride	$[(\text{CH}_3)_2\text{S}^+\text{CH}_2\text{CH}_2\text{COOH}]\text{Cl}^-$	Seaweed
Methioninemethylsulfonium chloride	$[(\text{CH}_3)_2\text{S}^+\text{CH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{COOH}]\text{Cl}^-$	Cabbage
2,2'-Dimercaptoisobutyric acid	$(\text{HSCH}_2)_2\text{CHCOOH}$	Asparagus
$\alpha$ -Terthienyl		Marigold petals
Biotin ( <i>q.v.</i> )		Yeast
Thiamine ( <i>q.v.</i> ) hydrochloride		Yeast and rice bran

alkyl methyl sulfide. Sulfuric acid is important to the detoxication of normal products of animal metabolism; and in protein metabolism, phenol and indoxyl are excreted as esters of sulfuric acid.

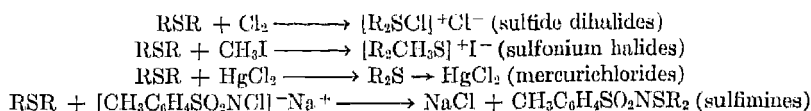
Among the types of sulfur compounds found in living organisms are mercaptans, disulfides, sulfides, sulfoxides, sulfones, esters of sulfuric acid, sulfonium compounds, isothiocyanates, and thiophenes. Some of these are listed in Table III.

*Sulfur Compounds of Petroleum.* Probably the largest processing operation involving organic sulfur compounds occurs in the petroleum industry (14). Inasmuch as sulfur compounds are detrimental in fuels from the standpoints of corrosion, odor, and effect on added tetraethyl lead, it is important to reduce the sulfur content as much as is practicable (see Vol. 10, p. 143). Crude petroleums have sulfur contents ranging from virtually zero to as high as 5 wt. %. The sulfur may be present in the form of hydrogen sulfide, elemental sulfur, thiols, disulfides, sulfides, and thiophenes. Sulfides are predominant in higher-boiling fractions, as indicated by the latest information. There is some question as to whether the disulfides and thiophenes are present in the original crude petroleum or whether they are the products of reactions occurring during the processing of the petroleum. Under the auspices of the American Petroleum Institute, a research project (1) is investigating the sulfur compounds of petroleum. As of July 1, 1953, 36 sulfur compounds boiling below 160°C. had been identified in a particular sample of crude oil. These included 14 thiols, 9 cyclic sulfides, and 13 alkyl sulfides.

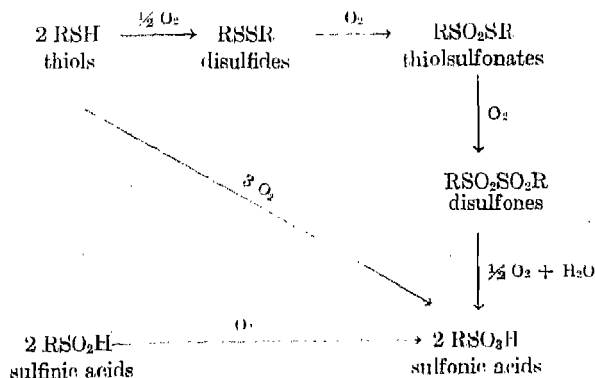
### Reactions

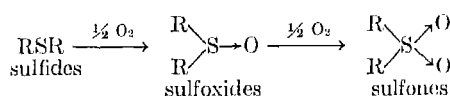
Only a brief summary of the reactions of organic sulfur compounds will be given (7,8,15), since fuller information is to be found in the separate articles on the more important classes of compounds.

*Addition to Sulfur Atom.* Because of the various valence states in which sulfur may exist, sulfur compounds are peculiarly susceptible to addition reactions. Sulfides react with halogens, with alkyl halides, with inorganic salts, and with chloramine-T:



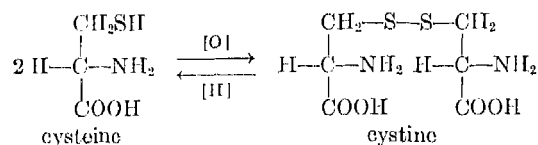
*Oxidation.* A special case of addition to the sulfur atom is that of oxidation, as in the first and last reactions above. Sulfur compounds have many possibilities for oxidative reactions:





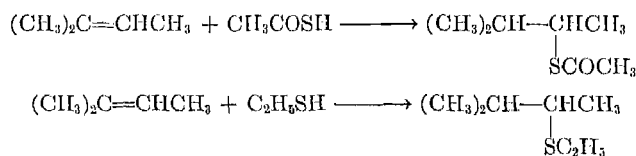
Oxidation may be brought about by a great variety of reagents, including air, halogens, hypohalites, nitric acid, concentrated sulfuric acid, elemental sulfur, potassium permanganate, and some peroxy compounds.

*Reduction.* Many of the oxidation reactions of sulfur compounds are reversible. The reduction of disulfides to thiols is relatively easy; one example in nature of a reversible oxidation-reduction system is that of cystine-cysteine:

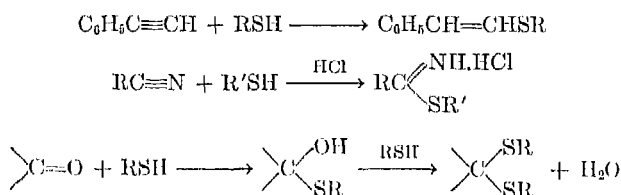


Thiolsulfonates may be reduced to mercaptans and sulfinic acids by zinc, zinc and acid, or hydrogen sulfide. Sulfoxides may be reduced to sulfides by sodium, zinc and acetic acid, hydriodic acid, phosphorus pentachloride, or hydrogen chloride. However, the sulfones and sulfonic acids are quite stable toward reducing agents.

*Reactions of Sulfur-Hydrogen Linkages.* Compounds containing the sulfur-hydrogen linkage (mercaptans, thiophenols, thiol acids, etc.) show acid properties. They react with bases or salts of heavy metals to give the corresponding salts (in the case of mercaptans, called mercaptides). Thiolic compounds add to double bonds, usually contrary to Markovnikov's rule because of the peroxides that are normally present. Examples are reactions of 2-methyl-2-butene with thiolacetic acid or ethane-thiol:

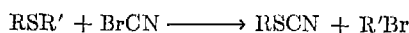


Addition also takes place with acetylenes, nitriles, and carbonyl compounds:

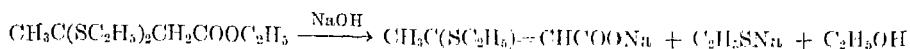


In the last reaction, if the carbonyl group is part of an aldehyde or ketone, the resulting products are mercaptals or mercaptoles. With carboxylic acids, the resulting compounds are thiol esters, and with  $\alpha,\beta$ -unsaturated ketones, esters, and acids,  $\beta$ -alkylthio derivatives are produced presumably by 1,4-addition.

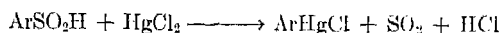
*Reactions of Sulfur-Carbon Linkages.* The sulfur-carbon linkage is generally quite strong unless it is subject to activation by some outside influence (16). One means of cleavage is with cyanogen bromide:



The presence of a labilizing group in the  $\beta$ -position to the sulfur permits ready cleavage of the sulfide in the presence of alkali, for example:



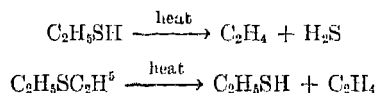
Oxidation of the sulfur changes the reactivity of the carbon-sulfur bond. Aromatic sulfonic acids may be hydrolyzed by heating with mineral acids to give sulfuric acid and the hydrocarbon. Fusion of salts of aromatic sulfonic acids with either alkali or potassium cyanide replaces the sulfonic acid group with OH or CN. Sulfinic acids may react with mercuric chloride to break the C—S bond:



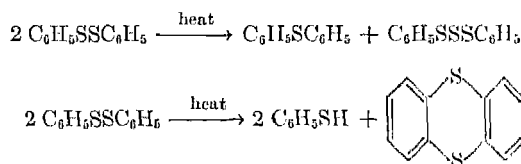
The breaking of C—S bonds by pyrolysis is discussed below.

*Reactions of Sulfur-Sulfur Linkages.* The sulfur-sulfur linkages are generally weak. Disulfides may be readily reduced to the thiol structure. The ease of oxidation-reduction is reflected in the difficulty of preparing pure unsymmetrical disulfides (4). As already noted, thiosulfonates are readily reduced to the mercaptans and sulfinic acids. Halogens react with disulfides to give sulfenyl halides. The di- and polysulfides may be heated with sulfur to form polysulfides that are richer in sulfur.

*Pyrolysis.* Pyrolysis of mercaptans results in hydrogen sulfide and the corresponding olefins, whereas sulfides decompose to give mercaptans and the olefins:



Disulfides have been reported to react either by disproportionation or by ring closure:



Upon pyrolysis, sulfonium salts or sulfonium hydroxides give sulfides and alkyl halides, or sulfides, olefins, and water. Some sulfonyl chlorides decompose on heating to give sulfur dioxide and alkyl halides. Pyrolysis of thioaldehydes or thioketones gives olefins and thiophene derivatives.

## Uses

Only a cursory review of the industrial uses of the many different types of organic sulfur compounds manufactured will be presented. In the pharmaceutical field, such compounds as the sulfa drugs (sulfanilamide, sulfathiazole), the germicide thimerosal (Merthiolate) and the sweetening agent saccharin (see 442) are well known. Various sulfur compounds are used as accelerators in rubber vulcanization, notable among them being thiuram disulfide and thiuram sulfide. Among the synthetic rubbers are the Thiokols, which are polymeric linear polysulfides. The various mustard gases (dichlorodiethyl sulfide and derivatives) were developed for wartime use. The detergent industry uses both sodium alkylarenesulfonates and sodium alkyl sulfates. Sodium formaldehydesulfoxylate,  $\text{NaSO}_2\text{CH}_2\text{OH}$ , is used as a reducing agent in vat

dyeing. Cellophane and viscose rayon are manufactured from cellulose through the intermediate formation of the cellulose xanthate.

### Classes

**Disulfides.** See *Sulfides, organic*.

**Heterocyclic Sulfur Compounds.** See *Heterocyclic compounds*.

**Isothiocyanates.** See *Thiocyanates and isothiocyanates, organic*.

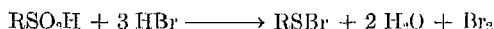
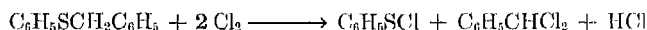
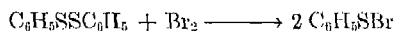
**Mercaptals and Mercaptoles.** See Vol. 8, p. 858.

**Mercaptans.** See Vol. 8, p. 858.

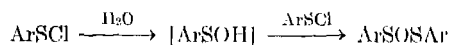
**Polysulfides.** See *Sulfides, organic*.

### Sulfenic Acid Derivatives.

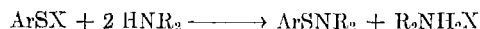
Only one compound of the formula  $\text{RSOH}$  is known—1-anthraquinonesulfenic acid—but numerous derivatives have been prepared (10). They include the sulfonyl halides, sulfonyl thiocyanates, sulfenamides, aryl and alkyl sulfenates, and sulfenic anhydrides. *Sulfonyl halides* may be prepared from mercaptans, disulfides, sulfides, and sulfinic acids:



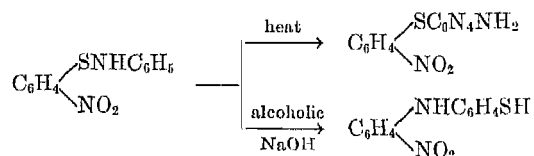
Sulfonyl halides may be hydrolyzed to give *sulfenic anhydrides*, which may be converted in the presence of excess alkali to disulfides and thiolsulfonic esters. The sulfenic acids are postulated as intermediates:



*Sulfenamides* are formed by the reaction of sulfonyl halides with ammonia or amines:



These compounds are of interest because of their usefulness as accelerators of rubber vulcanization (see *Rubber chemicals*). They have also been used as solid derivatives of amines. They undergo rearrangement to form sulfides when heated or to give diaryl-amines with alcoholic alkali:



2,4-Dinitrobenzenesulfonyl chloride has been used for characterization of alkenes, aromatic systems, alkynes, and alcohols (9).

**Sulfides.** See *Sulfides, organic*.

**Sulfines, Sulfilmines.**

The reaction of an *N*-chloroamide such as chloramine-T or chloramine-B with a sulfide produces a sulfine, such as *S,S*-diethyl-*N*-*p*-tolylsulfonylsulfine (R and R' = C<sub>2</sub>H<sub>5</sub>) (11):



They may also be prepared from tetramethylene sulfoxide, sulfonamides or substituted acetamides. The dialkyl sulfines have been reviewed by Challenger (5a).

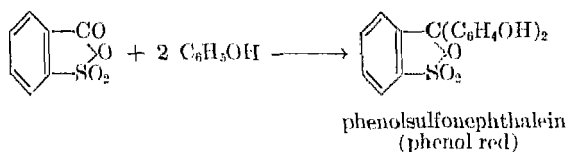
The sulfines are useful for characterization of the sulfides. Melting points of some of the chloramine-T adducts are: methyl sulfide, 158–159°C.; methyl ethyl sulfide, 133°C.; ethyl sulfide, 144°C.; isopropyl sulfide, 98°C.; *n*-butyl sulfide, 65.2°C. Sulfines derived from unsymmetrical sulfides are optically active.

**Sulfinic Acids** (*q.v.*).

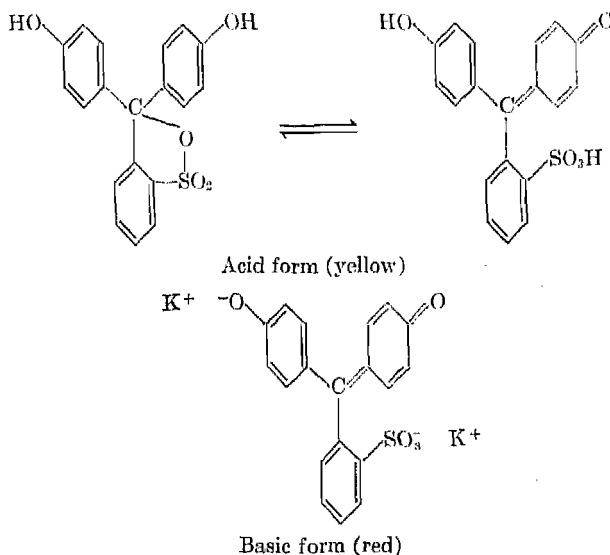
**Sulfonamides** (*q.v.*). See also *Sulfa drugs*.

**Sulfonephthaleins.**

Sulfur-containing compounds analogous to phenolphthalein (*q.v.*) are prepared by the condensation of a phenolic compound with *o*-sulfobenzoic anhydride:



Phenol, substituted phenols, and resorcinols have been reacted in this manner. The sulfonephthaleins find use as indicators (*q.v.*) through the changes from the acid form to the basic form:



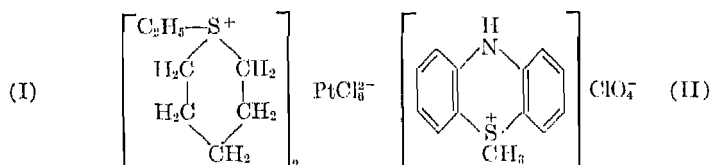
Phenolsulfonethalein is excreted by the kidneys, and retardation of excretion is recognized as an indication of kidney disability (15).

**Sulfones** (*q.v.*).

**Sulfonic Acids** (*q.v.*). See also *Sulfonation and sulfation*.

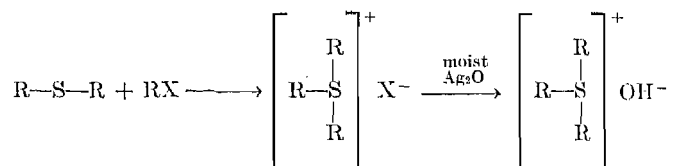
**Sulfonium Compounds, Thionium Compounds**,  $R_3S^+X^-$  (see also *Oxonium compounds*).

The older term "sulfines" for these compounds is objectionable because it suggests similarity to amines rather than ammonium compounds. The names of the compounds are formed by listing the radicals, followed by sulfonium and the inorganic radical, as, for example, dimethylisopropylsulfonium hydroxide. If the sulfur is in a ring (as thiapyran), the name of the ring compound may be utilized, that is, 1-ethyl-hexahydrothiapyrylium chloroplatinate (I), or the suffix -thionium in certain cases,

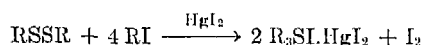


for example, 5,10-dihydro-5-methylphenazathionium perchlorate (II) derived from phenothiazine (see Vol. 7, p. 593).

Sulfonium compounds are formed by the reaction of sulfides with alkyl halides:

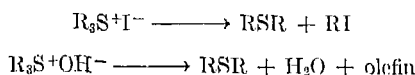


Treatment of the sulfonium halide with moist silver oxide or silver nitrate results in the sulfonium hydroxide or nitrate. Sulfonium salts have also been prepared from disulfides, thioaldehydes, and thioketones:

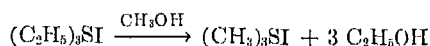


and from the reaction of sulfur or metallic sulfides with an excess of alkyl halide. Aryldialkylsulfonium salts are formed by the reaction of lead salts of thiophenols with alkyl sulfates. Triarylsulfonium salts may be obtained from phenols, thiophenols, or their ethers by the action of thionyl chloride and aluminum chloride, an aromatic sulfoxide, or a sulfinic acid and sulfuric acid.

Sulfonium compounds decompose upon distillation:

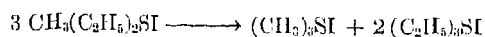


The ease with which the former reaction takes place is the key to several alkyl interchanges. Heating a sulfonium salt with an alcohol causes the radicals of the salt to be replaced by the radical of the alcohol:





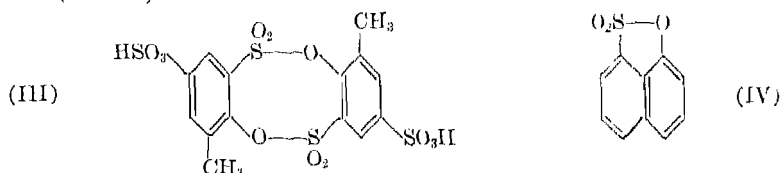
Unsymmetrical sulfonium salts may be converted to a mixture of the two or three corresponding symmetrical salts by heating:



Sulfonium halides form addition products with heavy-metal salts and with iodoform. Sulfonium hydroxides are strong bases and react with acids.

### Sulfonylides.

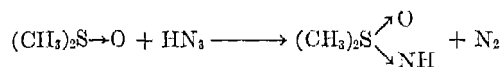
Sulfonylides are intermolecular esters of hydroxy sulfonic acids and are usually formed by heating a phenol or naphthol with oleum (ref. 15, p. 233). The sulfonylide of 6-methyl-1-phenol-2,4-disulfonic acid (2-hydroxytoluene-3,5-disulfonic acid), prepared from *o*-cresol and oleum, has the structure (III). It may also be named from the standpoint of the ring as 4,10-dimethylbenzo[1,5,2,6]dioxadithioein-2, 8-disulfonic acid 6,12-bis(dioxide).



### Sulfoxides (*q.v.*).

### Sulfoximines.

Compounds of the structure  $\text{R}_2\text{S}(\rightarrow\text{O})(\rightarrow\text{NH})$  have been prepared from the corresponding sulfoxide and sodium azide and sulfuric acid in chloroform solution:



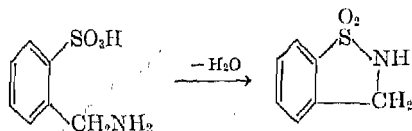
Sulfoximines of methyl sulfide, *n*-amyl sulfide, phenyl sulfide, methyl *p*-tolyl sulfide, *S*-methylcysteine, and methionine have been prepared. The last was found to be a toxic material in wheat flour bleached with nitrogen trichloride (5) (see also Vol. 3, p. 623).

### Sulfur Dyes (*q.v.*).

**Sulfuric and Sulfurous Esters (*q.v.*).** See also *Sulfonation and sulfation*.

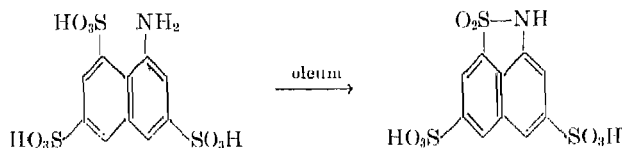
### Sultams.

Sultams are intramolecular condensation products derived from amino sulfonic acids and having the grouping  $\text{—SO}_2\text{NH—}$ :



They are analogous to the lactams (*q.v.*) and are similarly named from the heterocyclic system; thus the compound above would be 2,3-dihydrobenzisosulfonazole or

1,2-benzisothiazoline 1,1-dioxide (the 3-oxo derivative is saccharin). The sultams may be prepared by the action of oleum on amino sulfonic acids (15):

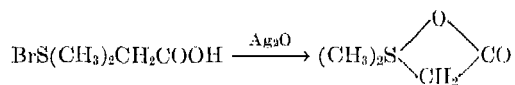


### Sultones.

Sultones are intramolecular esters of hydroxy sulfonic acids and are analogous to lactones (*q.v.*). They may be named as the sultone of the appropriate acid, as a sultone, or as a heterocyclic derivative. Thus the sultone (IV) of 1-hydroxy-8-naphthalenesulfonic acid may be named as such, as 1,8-naphthosultone, or as 2-naphth[1.8-*cd*]-isothiazole 1,1-dioxide. These compounds are generally prepared by the action of oleum on the phenol or naphthol.

### Thetins, Thiobetaines.

These compounds have the structure  $R_2S.O.CO.CH_2$  and are named as derivatives of thetin, for example, 2,2-dimethylthetin. They may also be regarded as inner sulfonium salts analogous to the betaines (*q.v.*), and other (not inner) sulfonium salts have sometimes been called *thetine salts*. Thetins may be prepared from the appropriate sulfide and bromoacetic acid:



The methyl derivatives have recently attracted attention as methylating agents in biological processes.

**Thiazines.** See *Azine dyes*, Vol. 2, p. 221; *Heterocyclic compounds*, Vol. 7, p. 453.

**Thiazoles.** See *Heterocyclic compounds*, Vol. 7, p. 441; *Thiazole dyes*.

**Thioacetals.** See *Mercaptals*.

**Thio Acids** (*q.v.*).

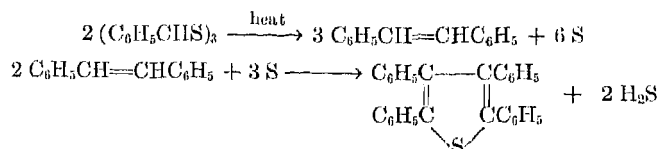
### Thioaldehydes (Thials) and Thioketones (Thiones).

Thioaldehydes and thioketones (4a) are very prone to polymerize so that isolation of monomers is difficult. In this respect, they differ considerably from the corresponding oxygen compounds. The thiocarbonyl group,  $>C=S$ , is a potent chromophore, and monomers are highly colored (red to blue); however, the polymers are colorless. The compounds of low molecular weight have very disagreeable odors. Thiourea,  $NH_2CSNH_2$ , is the best known of the thiocarbonyl compounds.

The nomenclature of thioaldehydes and thioketones is similar to that used for their oxygen analogs except that the terms "thial" and "thione" are used instead of "al" and "one" (or "ketone"), or "thioformyl" and "thioxo" instead of "formyl" and "oxo" (or "keto"). In the case of many common names, the prefix "thio" is used, as

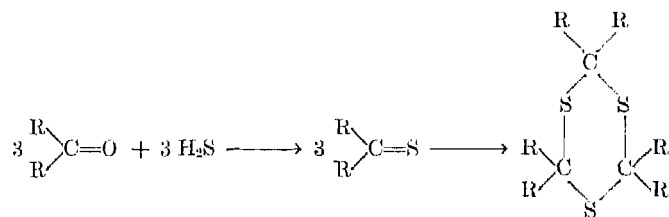
in thioacetaldehyde, thiobenzaldehyde, and thioacetone. Cyclic polymers can also be named as heterocyclic compounds.

Oxidation of the cyclic trimers proceeds like that of other sulfides, giving sulfoxides and sulfones. The monomeric thioketones are oxidized to ketones and sulfur dioxide by the action of hydrogen peroxide. Upon pyrolysis, thioaldehydes and thioketones give olefins and thiophene derivatives, the latter probably by reaction of free sulfur with the olefin:

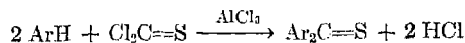
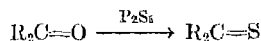
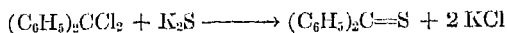


The thioaldehydes and thioketones react with alkyl iodides to form sulfonium salts. Addition products with heavy metals, such as mercury, platinum, and silver, are formed by the mono-, di-, and trimeric derivatives. Thioketones are hydrolyzed to ketones and hydrogen sulfide by heating with dilute alkali. Thioketones react with carbonyl reagents.

The compounds may be prepared by the action of hydrogen sulfide on the corresponding aldehyde or ketone, usually with an acid or zinc chloride catalyst:



Other preparative methods include the interaction of methylene halides with metal sulfides or thioacetic acid, and of ketones with phosphorus pentasulfide or ammonium hydrosulfide. Diaryl thioketones may be prepared by the Friedel-Crafts reaction, using thiophosgene.



**Thiocyanates.** See *Thiocyanates and isothiocyanates, organic*.

**Thioethers.** See *Sulfides, organic*.

**Thioindigoid Dyes.** See *Indigoid dyes*, Vol. 7, p. 823.

**Thioketones.** See "Thioaldehydes."

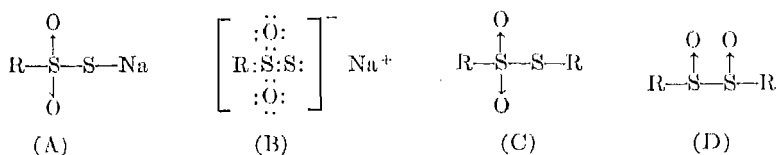
**Thionium Compounds.** See "Sulfonium compounds."

**Thiophene and Derivatives.** See *Thiophene*.

**Thiosulfonates, Thiolsulfonates.**

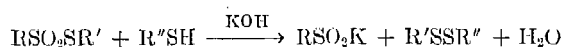
Thiosulfonic acids are unknown, but their salts and esters may be prepared. The usual structure given for the salts is that shown in (A); but the electronic struc-

ture shown in (B) indicates the impossibility of designating them as either thiol-sulfonates or thionosulfonates. However, as the usual reactions of the esters can be



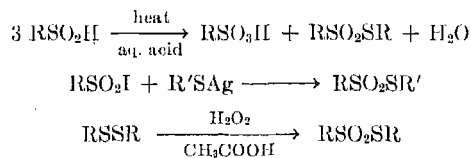
explained on the basis of the thiol-sulfonate structure (C), it is fairly well accepted and names such as 2,5-dichlorophenyl 2,5-dichlorobenzenethiol-sulfonate are used. Some explanations of properties of symmetrical esters (notably optical rotation) have been based on the isomeric disulfoxide formula (D).

Upon hydrolysis with dilute aqueous alkali, or reaction with thiolic compounds, thiol-sulfonates give sulfinates and disulfides:



Reaction with Grignard reagents gives sulfonates and sulfides. The thiol-sulfonates may be oxidized to either disulfones or sulfonic acids. Upon reduction, they give sulfinates and thiols.

The thiol-sulfonates may be prepared from sulfinic acids, from sulfonyl halides, and from disulfides:



**Thiosulfuric Ester Salts.** See *Thiosulfuric acid*.

**Thiourea and Derivatives.** See *Urea*.

**Thiuram Sulfides.** See *Rubber chemicals*.

**Xanthic Acids and Xanthates** (*q.v.*).

### Bibliography

- (1) Ball, J. S., Bordwell, F. G., Smith, H. M., Waddington, G., and Seyfried, W. D., *Proc. Am. Petroleum Inst.*, **32**, Pt. III, 139 (1952).
- (2) Bull, J. S., and Haines, W. E., *Chem. Eng. News*, **24**, 2765 (1946).
- (3) Birch, S. F., *J. Inst. Petroleum*, **39**, 185 (1953).
- (4) Birch, S. F., Cullum, T. V., and Dean, R. A., *J. Inst. Petroleum*, **39**, 206 (1953).
- (4a) Campaigne, E., *Chem. Revs.*, **39**, 1-77 (1946).
- (5) Challenger, F., *Endeavour*, **12**, 173 (1953).
- (5a) Challenger, F., *Science Progr.*, **41**, 593 (1953).
- (6) Challenger, F., "The Sulphur Compounds of Bituminous Oils," in Dunstan, *et al.*, *Science of Petroleum*, Oxford Univ. Press, London, 1938, Vol. II, pp. 1042-46.
- (7) Connor, R., "Organic Sulfur Compounds," in Gilman, *Organic Chemistry*, 2nd ed., Wiley, N.Y., 1943, Vol. I, pp. 835-943.
- (8) Fuson, R. C., *Advanced Organic Chemistry*, Wiley, N.Y., 1950, pp. 573-86.
- (9) Kharasch, N., and Buess, C. M., *J. Am. Chem. Soc.*, **70**, 2742 (1949); **72**, 3529 (1950); **74**, 3422 (1952); **75**, 1081 (1953); **75**, 2658 (1953).
- (10) Kharasch, N., Potempa, S. J., and Wehrmaister, H. L., *Chem. Revs.*, **39**, 269 (1946).

- (11) Mann, F. G., and Pope, W. J., *J. Chem. Soc.*, **121**, 1052 (1922).
- (12) Patterson, A. M., Capell, L. T., and Magill, M. A., *C.A.*, **39**, 5875 (1945).
- (13) Reid, E. E., "The Sulphur Compounds in Petroleum," in Dunstan *et al.*, *Science of Petroleum*, Oxford Univ. Press, London, 1938, Vol. II, pp. 1033-41.
- (14) Seyfried, W. D., *Chem. Eng. News*, **27**, 2482 (1949).
- (15) Suter, C. M., *Organic Chemistry of Sulfur*, Wiley, N.Y., 1944.
- (16) Tarbell, D. S., and Harnish, D. P., *Chem. Revs.*, **49**, 1 (1951).
- (17) Wheland, G. W., *Advanced Organic Chemistry*, 2nd ed., Wiley, N.Y., 1949, pp. 355-61.

J. S. BALL

**SULFUR DIOXIDE, SO<sub>2</sub>.** See *Sulfur compounds, inorganic*.

## SULFUR DYES

Although sulfur is present in many classes of dyes (*q.v.*), those classed as sulfur dyes or *sulfide dyes* not only contain sulfur but are also soluble in a 0.25-0.50% sodium sulfide solution, from which they are then capable of dyeing cotton. The sulfur dyes are further characterized by the intermediates from which they are manufactured. These intermediates are mainly aromatic polyamines or hydroxy amines. The amine group may be either primary, secondary, or tertiary, or any equivalent group such as nitro, nitroso, or imino. Although the manufacture of sulfur dyes is limited to the use of specific starting materials, nearly all aromatic polyamines and hydroxy amines or their equivalents will produce sulfur dyes under appropriate conditions. There are some notable exceptions to this rule, most important of which is the formation of a brown dye from cresylic acid. On the other hand, certain intermediates like *p*-phenylenediamine, *p*-nitroaniline, and benzidine do not form sulfur dyes under ordinary conditions but are used in conjunction with other intermediates. Their presence in a sulfur melt increases the reactivity of sulfur with other intermediates.

The selection of a particular starting material for any color is based on economics and on the resultant fastness of the dye to oxidation by sodium hypochlorite solution. Economics plays the bigger part, since the continued use of sulfur colors is based on the low cost of their tinctorial power per weight of dyed cotton. Their costs are between 10 and 30% of all other types of dyes that impart a comparable intensity of color to cotton fiber. See also *Dyes (application)*, Vol. 5, p. 386.

**History.** Sulfur dye chemistry was still emerging from empiricism as late as the turn of the twentieth century. There are two periods in the development of sulfur colors.

*The first period* (1873-1893) began with the discovery of a brown dye by Croissant and Bretonnière, and ended with the discovery of a black dye by Vidal. Croissant used sawdust, cellulose, and animal skins as starting materials; Vidal used *p*-aminophenol. The dyes made in this period were not true sulfur colors. They were made mostly from aliphatic compounds and were regarded as inferior dyes. Chemists working on other dyes passed along any troublesome tarry by-products to the dye chemists working with sulfur, who were called upon to make sulfur colors from these and every by-product for which no other use could be found. Inasmuch as the chemical constitution of sulfur dyes was not known, it was not considered necessary for the chemist to know what his starting material consisted of. This idea exerted a considerable influence on the new period to follow and has not been completely discarded even today. The following is a list of the starting materials known to be used during this period: sawdust, humus, lichens, mosses, brans, farina, gluten, starch, sucrose, glucose, tannin, gallic acid, gelatin, casein, albumin, blood, horn, feathers, aloes, resins, gums, soot, paper waste, cotton waste, vegetable detritus, and cellulose.

*The second period* (1893-) was initiated by the discoveries of Vidal, whose work led to the

realization that sulfur dyes were definite colors which could be made from specific intermediates. Most of our basic knowledge of sulfur colors today dates back to the first 10 years or so of this period, during which Vidal pointed out new raw materials and attempted to explain the chemical structure of sulfur colors. Every possible intermediate was tested and used in the early part of this second period, and many of them are economically important today. From January 1, 1900 to January 1, 1902, there was a boom in sulfur colors, and in the space of these two years more than 200 patents were issued on their manufacture. Another pioneer in the second period, working for the most part after 1900, was Herz, who developed most of the sulfur blues and greens known today.

The list of acceptable intermediates today is a selection made from several hundreds of aromatic compounds containing at least one hydroxyl and one amino group (or its equivalent), and to a lesser extent aromatics containing two or more amino groups without any hydroxyl group. This list includes all indophenols, amino phenols (*q.v.*), azines (*q.v.*), hydroxydiphenylamines, arylenediamines (see *Phenylenediamines*), and naphthylamines (*q.v.*), and their sulfonic acids. Indophenol, as used in the dye industry, is a class name including all *N*-(*p*-aminoaryl)-*p*-quinonemonoimine structures, of which the indoanilines are an important part.

### Chemical Structure

Sulfur colors are colored amorphous powders insoluble in either water or solvents and, therefore, cannot be isolated in pure form for a study of their chemical structure. Moreover, a mixture of dye molecules that cannot be separated is obtained from the reactions forming a sulfur color.

The mechanism of the reaction whereby sulfur atoms are introduced into an organic compound through the reaction of sulfur or sodium polysulfide with the liberation of hydrogen sulfide is similar to that of the introduction of oxygen atoms into an organic compound by means of oxygen or sodium peroxide with the liberation of water.

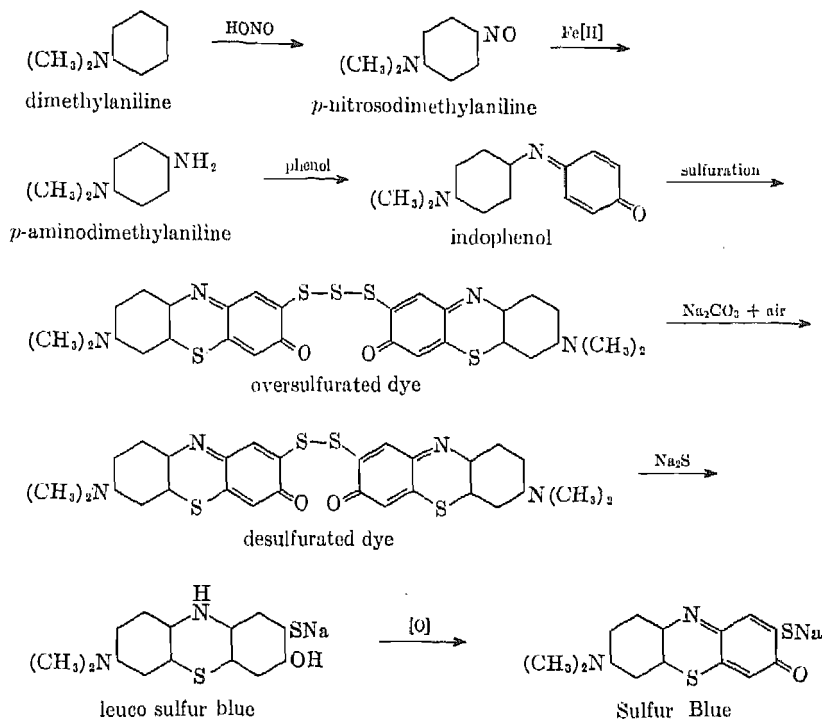
All sulfur dyes contain sulfide groups, which may be in the form of chains bridging two molecules of the dye intermediate,  $R-S_n-R$ , or of open chains,  $R-S_n-S$  (the manner of termination of such chains is uncertain), or of mercapto groups,  $R-SH$ . In the manufacture of the dyes they are often first oversulfurated and then desulfurated, and before being used they are dissolved in sodium sulfide solution. The desulfuration (and perhaps also the dissolution in sodium sulfide before dyeing) removes some sulfur atoms from the long chains and reduces some of them to mercapto groups so that the dye becomes soluble as  $R-SNa$ . The number of sulfur atoms per mole of intermediate is probably never less than 1, and rarely exceeds 5; frequently there are about 3 atoms of sulfur to 2 molecules of the intermediate. The sulfur bridges and chains are auxochromic, and their variable length is an important factor determining the shade of any one color obtained. In general, sulfur dyes are not pure chemical compounds, and in any formula given for a sulfur dye the presence of a variable number of sulfur atoms in these bridges and chains is to be understood.

Investigators have estimated the probable length of these chains in the oversulfurated intermediates, with the maximum length 8 atoms of sulfur. Such long chains are frequently referred to as "loosely bound" sulfur, because they are easily shortened by desulfuration. In certain methods of desulfuration employing metallic catalysts (see p. 463), a further change is believed to take place in the monosulfide groups through addition of oxygen to the sulfur.

Although sulfur dyes dissolve in alkaline solutions in the presence of reducing agents (the universal solvent being sodium sulfide), they revert to their insoluble form by oxidation with air. This mechanism of reduction and oxidation in a sulfur dye, however, does not reveal any information about its structure. Very few formulas, therefore, have been proposed, and in only one color has the chemical structure been

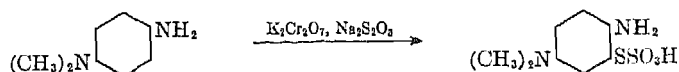
elucidated, namely, a sulfur blue made from the indophenol obtained from *p*-aminodimethylaniline and phenol. The chemical reactions leading to the formation of this blue dye are shown in Scheme 1.

SCHEME 1

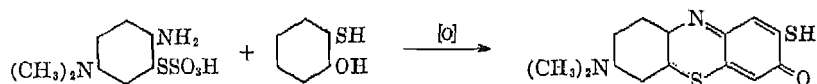


Actually, as in the case of many other sulfur dyes, the formation of this dye is completed at the time of solution in sodium sulfide to form the mercaptan group.

The formula of this sulfur blue was proved by its preparation by an entirely different synthesis. In a reaction characteristic of diamines, *p*-aminodimethylaniline is treated with potassium dichromate and sodium thiosulfate to yield a thiosulfuric acid ester:



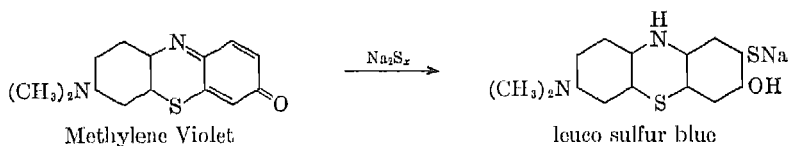
When the 2-amino-5-dimethylaminophenyl hydrogen thiosulfate thus formed is oxidized in an alkaline solution in the presence of *o*-hydroxythiophenol (*o*-mercaptophenol), a mercaptan is formed which is identical in properties to the sulfur blue described above:



The formation of the thiazine ring in either synthesis is proved by the conversion of either product to Tetrabromomethylene Violet in a reaction similar to that used on

Methylene Violet obtained from Methylene Blue (*C.I.* 922), which is known to have a thiazine ring structure (see Vol. 2, p. 221).

As might be expected, Methylene Violet, if sulfurated with sodium polysulfide, will yield the same sulfur blue:

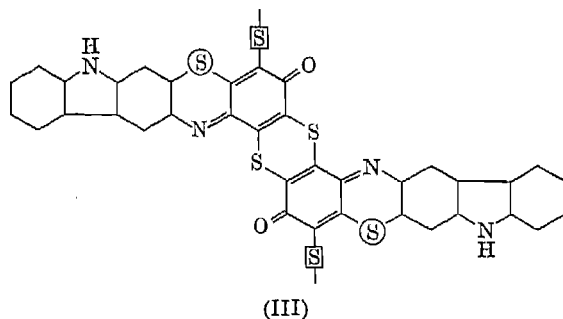


Another sulfur blue, closely related to the blue color described above, is produced by sulfuration of the indophenol obtained from the combination of *o*-toluidine and *p*-aminophenol. The formula, in part, might be represented by structure (I).



The formation of the thiazine ring in this case is similar to the previous example, but the position of the sulfide chain is not certain. The points of entry for sulfur atoms are generally thought to be ortho to the auxochrome groups, such as OH, NH<sub>2</sub>, SO<sub>3</sub>H. However, if one of these positions is also ortho to the carbon bearing the thiazine sulfur, it is rarely filled by sulfur except under stress of the strongest kind of sulfuration. In formula (I) two of these vacant positions are blocked, leaving one choice for entrance of sulfur in the position ortho to the auxochromic quinone oxygen. The disulfide in formula (I) serves as the bridge to another molecule, but it is not known whether the CH<sub>3</sub> group in this color serves as the nucleus for the formation of a thiazole group between two of the molecules of the intermediate. If the CH<sub>3</sub> group is absent, as is the case if aniline instead of *o*-toluidine is used, then the dye formed is represented, in part, by formula (II). It is a greener shade of the blue dye which is probably not manufactured. A greener shade can also be made by oversulfuration of the blue dye from *o*-toluidine; by desulfuration of the green shade from aniline the blue dye is obtained. These are not exceptional cases since the shade of most sulfur dyes can be altered over such a wide range that one color runs into another color.

Hydron Blue (*C.I.* 969), at present the most important blue sulfur dye competing with indigo, is not, strictly speaking, a true sulfur dye, since it is vatted with sodium hydrosulfite, Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub>, instead of sodium sulfide. Its probable constitution is that of a

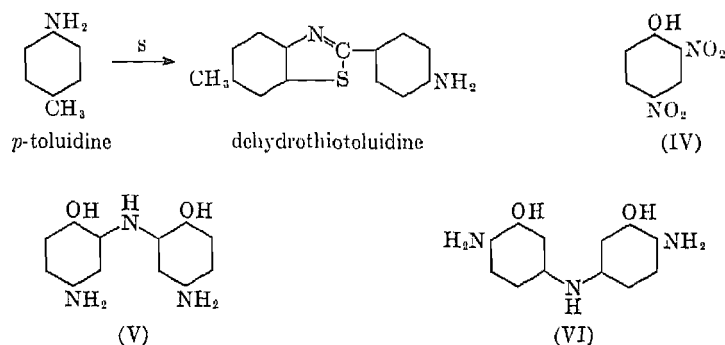




thiazine substituted with disulfide groups. Starting with two moles of the indophenol obtained from carbazole,  $\text{C}_6\text{H}_4\text{NH.C}_6\text{H}_4$ , and *p*-nitrosophenol,  $\text{HO.C}_6\text{H}_4\text{N:O}$  (see p. 456),

the addition of sulfur to form the thiazine rings and the disulfide groupings is shown in (III). *N*-Ethylcarbazole in place of carbazole as a starting material produces greener shades of Hydron Blue (see p. 452).

Thus it can be stated with reasonable certainty from the examples cited that all sulfur colors made from indophenols, indamines, or diphenylamines contain thiazine rings formed by the introduction of sulfur ortho to nitrogen. In other sulfur colors derived from the alkylarylenediamines, such as brown, yellow, and orange dyes from toluene-2,4-diamine, the formation of the thiazole group by interaction with sulfur is the source of an important chromophore. The formation of thiazole groups is best illustrated by the reaction of *p*-toluidine with sulfur to yield dehydrothio-*p*-toluidine among other products (see *Thiazole dyes*).



Most of the sulfur browns, red browns, bordeauxs, yellows, and oranges contain the characterizing thiazole group. The presence of a methyl group in the starting materials of these dyes is necessary for the formation of such a group. It is almost certain that these dyes contain thiazine groups in addition to the thiazole group.

Many sulfur dyes are not made directly from the original starting material used in the fusion, but from a new intermediate formed by the action of sodium polysulfide. An example of this is Dinitrophenol Sulfur Black. The starting material is 2,4-dinitrophenol (IV), but the actual intermediate required for making this color is the diamino-dihydroxydiphenylamine (V or VI) formed from the dinitrophenol by the action of sodium polysulfide in either a water or ethyl alcohol medium, and accompanied by the evolution of ammonia. If a *n*-butyl alcohol (1-butanol) medium is used, only the *o*-nitro groups are reduced, no ammonia is evolved, and no sulfur black is formed. These facts would tend to support formula (VI) for the diphenylamine intermediate which produces sulfur black. Considerable uncertainty exists, therefore, about the actual intermediate product which forms this sulfur black. Although it is known that approximately  $\frac{1}{2}$  mole of ammonia and 1 mole of hydrogen sulfide are evolved during the fusion and that the dye receives about  $1\frac{1}{2}$  moles of sulfur per mole of dinitrophenol, the actual formula of this black dye remains the subject of much speculation. It is generally agreed, however, that 1 sulfur atom forms a thiazine structure with the secondary amino group of the diphenylamine compound and that the color involves the formation of several bridged molecules connected by sulfur chains.

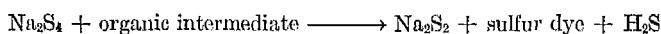
### Manufacture

The manufacture of sulfur dyes is an art rather than a science, and the introduction of sulfur into an organic intermediate as well as the removal of excess sulfur requires skill and experience beyond that described in a process. Many of the essential details of manufacturing are known by relatively few operators and manufacturers.

#### SULFURATION AND OVERSULFURATION

The introduction of sulfur into a chemical intermediate for the manufacture of a sulfur dye is called a **fusion** and is referred to as *sulfuration* or *thionation*. The two practical sulfuration agents are sulfur and sodium polysulfide. The intermediate must be soluble in either of these agents, or soluble, with the agent, in a common solvent. When sulfur is the medium of fusion, it usually serves as the solvent for the intermediate, but, in certain cases where the intermediate is insoluble in sulfur, the presence of some other intermediate, such as *p*-phenylenediamine, *p*-nitroaniline, or benzidine, serves as an activator. Fusion with sulfur alone is called *baking* because it is conducted in the dry state at high temperatures, usually 200–300°C. Fusion with sodium polysulfide is also a baking process when carried out in the fused state at high temperatures, though it is not a dry process, because the sodium polysulfide retains some water even at high temperatures. Some dyes are made by baking with sulfur and then with sodium polysulfide.

The most frequently used method of sulfuration is the *reflux fusion with sodium polysulfide*, using either water, ethyl alcohol, or 1-butanol as solvent. Other alcohols may be used as reflux mediums, but reflux temperatures of 78°C. (ethyl alcohol) and 109°C. (95% butanol with sodium polysulfide) are adequate for colors requiring either a low or a high temperature. The reflux temperatures employed in sodium polysulfide aqueous fusions are important because they determine the concentration of the polysulfide solution, and they vary from 102 to 115°. Aqueous polysulfide fusions may reach temperatures as high as 160°C. under pressure.



The sodium polysulfide ratio for all types of fusions and all starting intermediates may range from  $\text{Na}_2\text{S}_3$  to  $\text{Na}_2\text{S}_8$ . The preferred ratios are  $\text{Na}_2\text{S}_4$  and  $\text{Na}_2\text{S}_{4.5}$ , and the moles required per mole of intermediate may vary from about  $1\frac{1}{2}$  to  $4\frac{1}{2}$  moles. Below  $\text{Na}_2\text{S}_3$  there is little likelihood of any appreciable amount of sulfur leaving the polysulfide for reaction with the organic intermediate.

The time required to complete a fusion may vary from about  $1\frac{1}{2}$  to 100 hr., and even up to 150 hr. The processes using long fusion times can be shortened by using a metal catalyst, a higher sulfur ratio in the sodium polysulfide, or a higher fusion temperature. A change from aqueous medium to a high-boiling alcohol may also be indicated where aqueous fusions require too long a fusion time.

Which type of fusion should be used, whether with sulfur or with sodium polysulfide in either a water or alcohol medium, cannot always be predicted but must be determined by actual trials. Some intermediates which decompose in aqueous fusions will produce good colors in alcohol. Other intermediates which require the water type of fusion will not, as a rule, produce a satisfactory color in butanol, and in some cases no color at all is formed (see p. 449). Table I gives the intermediates and types of fusion used for several sulfur dyes.

TABLE I. Intermediates and Types of Fusion for Various Sulfur Dyes.

Color	C.I. number	Intermediate	Type of fusion used
Brown	940	1,8-Dinitronaphthalene	Polysulfide baking
Brown	—	3,6-Diamino-2,7-dimethylacridine	Sulfur and polysulfide baking
Brown	948	2,4-Dinitrotoluene drip oil	Sulfur baking
Brown	—	Cottonseed meal and 1-chloro-2,4-dinitrobenzene	Polysulfide baking
Brown	—	<i>p</i> -Nitrosodimethylaniline, 2,4-dinitrotoluene, and <i>p</i> -nitroacetanilide	Polysulfide baking
Brown	548 <sup>a</sup>	Cresylic acid	Polysulfide baking
Cutch brown	948	2,4-Dinitrotoluene	Polysulfide baking
Tan	—	<i>p</i> -Nitrosodimethylaniline, 2,4-dinitrotoluene, 2,4-dinitrobenzene, and <i>p</i> -nitroaniline	Polysulfide baking
Tan	948	Toluene-2,4-diamine and <i>p</i> -nitroaniline	Sulfur baking
Tan	948	Toluene-2,4-diamine	Sulfur baking
Yellow brown	948	2,4-Dinitroacetanilide and 2,4-dinitrotoluene	Polysulfide baking
Yellow brown	948	Toluene-2,4-diamine and <i>p</i> -nitroaniline or <i>p</i> -phenylenediamine	Sulfur baking
Yellow brown	948	Toluene-2,4-diamine and benzidine base	Sulfur baking
Orange	948	Toluene-2,4-diamine	Sulfur baking
Orange	948	Toluene-2,4-diamine and <i>p</i> -phenylene diamine	Sulfur baking
Yellow	951	Mono- and diformamides of toluene-2,4-diamine	Sulfur baking
Yellow	951	Mono- and diformamides of toluene-2,4-diamine and <i>p</i> -phenylenediamine	Sulfur baking
Yellow	951	Mono- and diformamides of toluene-2,4-diamine and benzidine base	Sulfur baking
Yellow	951	Mono- and diformamides of <i>p</i> -toluidine, toluene-2,4-diamine, benzidine base, and aniline	Sulfur baking
Yellow	953	2,4-Dinitroacetanilide	Polysulfide baking
Yellow	955	<i>p</i> -Toluidine and benzidine base	Sulfur baking
Blue	285 <sup>a</sup>	Indophenol from diphenylamine-4-monosulfonic acid ( <i>N</i> -phenylsulfanilic acid) and <i>p</i> -aminophenol	Polysulfide-water reflux
Blue	956	4-Hydroxy-2',4'-dinitrodiphenylamine (from 1-chloro-2,4-dinitrobenzene and <i>p</i> -aminophenol)	Polysulfide-water reflux
Blue	—	Indophenol from diphenylamine-2-carboxylic acid ( <i>N</i> -phenylanthranilic acid) and <i>p</i> -nitrosophenol	Polysulfide-water reflux
Blue	957	Indophenol from <i>p</i> -aminodimethylaniline and phenol (see p. 447)	Polysulfide-water reflux
Blue	959	Indophenol from <i>o</i> -toluidine and <i>p</i> -nitrosophenol	Polysulfide-water reflux
Blue	969	Indophenol from carbazole and <i>p</i> -nitrosophenol	Polysulfide-butanol reflux

(Continued)

TABLE I. Intermediates and Types of Fusion for Various Sulfur Dyes (*Concluded*).

Color	C.I. number	Intermediate	Type of fusion used
Blue black	970	Indophenol from carbazole and <i>p</i> -nitrosophenol	Polysulfide-butanol reflux
Blue	971	Indophenol from <i>N</i> -ethylcarbazole and <i>p</i> -nitrosophenol	Polysulfide-butanol reflux
Black	978	2,4-Dinitrophenol	Polysulfide-water reflux
Black	978	2,4-Dinitrophenol and picric acid	Polysulfide-water reflux
Black	126 <sup>a</sup>	<i>p</i> -Hydroxyphenyl-2-naphthylamine	Polysulfide-butanol reflux
Olive	1002	<i>p</i> -Nitrosophenol	Polysulfide-water reflux
Green	1006	Indophenol from <i>N</i> - <i>p</i> -tolyl-1-naphthylamine-8-sulfonic acid and <i>p</i> -aminophenol	Polysulfide-water reflux
Green	1006	Indophenol from <i>N</i> -phenyl-1-naphthylamine-8-sulfonic acid and <i>p</i> -aminophenol	Polysulfide-water reflux
Blue green	1006	Indophenol from 1-naphthylamine-6-sulfonic acid and <i>p</i> -aminophenol	Polysulfide-water reflux
Violet	1008	7-Amino-9-phenylphenazone-2 (phenosafrinone)	Polysulfide-water reflux
Bordeaux	1012	Phenazine derivative (from toluene-3,5-diamine and <i>p</i> -aminophenol)	Polysulfide-water reflux
Red brown	1012	Phenazine derivative (from toluene-3,5-diamine and <i>p</i> -aminophenol)	Polysulfide-water reflux
Corinth	1012	Phenazine derivative (from toluene-3,5-diamine and <i>p</i> -aminophenol)	Polysulfide-water reflux

<sup>a</sup> These numbers are Prototype numbers listed in the A.A.T.C.C. *Technical Manual and Year Book*.

In all sulfur color fusions, hydrogen sulfide gas is evolved. As the reaction is reversible, the hydrogen sulfide gas must have a free and easy exit. Pressure fusions should be bled to allow hydrogen sulfide to escape. All reflux fusions, whether in alcohol or water, should be provided with large-diameter reflux condensers so that the return condensate does not trap the escaping gas. Certain dyes, particularly the greens made from the indophenols obtained from phenyl- or tolynaphthylamine-sulfonic acids and *p*-aminophenol, are so easily reversed by hydrogen sulfide that, if there is too much free space above the fusion melt, the process may fail because of the higher concentration of hydrogen sulfide.

Unless sulfuration is pushed beyond theoretical proportions, there is always a portion of the dye which never acquires its normal amount of sulfur. Undersulfuration for even a small portion of a sulfur dye is the chief cause of dullness in shade. Only by continuing the sulfuration beyond theoretical proportions and then reversing the process to remove excess sulfur can accurate control of the shade of color be obtained.

#### DESULFURATION

More important than the introduction of sulfur into the dye molecule is the subsequent removal of excess sulfur (desulfuration). This operation not only removes excess sulfur from the dye molecule but also enables the operator to obtain a better control of the shade and brightness of the dye. Some manufacturers attempt to obtain the desired shade and brightness by direct fusion without resorting to desulfura-

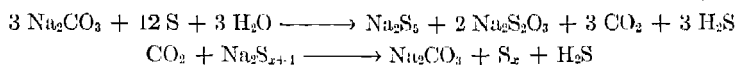
tion, but this procedure is not nearly so successful as oversulfuration followed by desulfuration, inasmuch as control of sulfur flow is more positive in desulfuration than in sulfuration.

The following methods are most frequently employed in desulfuration:

**Control of the time of drying** by adjustment of the amount of air circulating during drying, and regulation of the temperature. Repasting the dye with water for redrying is sometimes resorted to if the dye failed to get the expected amount of desulfuration from the first drying operation.

**Air-blowing of the dye** in an aqueous suspension at various temperatures, with or without the addition of sodium hydroxide, sodium carbonate, or sodium sulfide, and with or without the presence of iron, copper, or manganese.

**Addition of a small quantity of sodium carbonate** to aqueous sodium polysulfide reflux or pressure fusions. Although not strictly considered a desulfuration, this procedure acts as a retarder for the sulfuration and will produce a shade of color corresponding to a lower degree of sulfuration. The effect of sodium carbonate is explained by its reaction with sulfur to liberate hydrogen sulfide, which increases the mass action reversible feature of the hydrogen sulfide normally evolved by the fusion process. It thus slows down the progress of a normal fusion and is found particularly effective in causing redder shades for the sulfur blacks made from dinitrophenol.



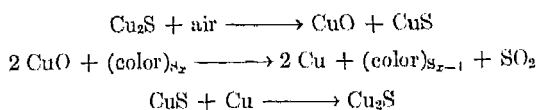
**Sodium sulfite treatment** of an aqueous suspension of the sulfur dye at about 70°C., an effective way to remove sulfur from a sulfur dye. One mole of sodium sulfite can remove one mole of free or loosely bound sulfur through the formation of sodium thiosulfate.

**Fusion of the dye with sodium sulfide**, or drying the dye in contact with sodium sulfide, which combines with sulfur to form the disulfide. The presence of air will convert the sodium disulfide to sodium thiosulfate, with the sulfur dye acting as an oxygen carrier. In several instances, exceptions are to be found, most notably in the case of Sulfur Black (*C.I.* 978) manufacture, where a sodium sulfide treatment in the drying stage protects the dye from further desulfuration and oxidation, resulting in the greener shades, which rate approximately 15% more tinctorial strength.

#### ACTION OF METALS

The presence of metals in sulfur dye fusions influences the shade and yield of colors obtained. This metallic influence, however, has been found advantageous in relatively few colors, and the choice of a metal for addition to the sulfuration or desulfuration has been limited to copper, manganese, and iron. On the other hand, each dye must be made either in a lead apparatus if adversely influenced by iron, or in brick-lined apparatus if lead is also detrimental. Where copper is used as a catalyst, a lead apparatus should be used.

The action of polyvalent metals in accelerating the introduction of sulfur into an intermediate during sulfuration, or of oxygen during desulfuration, can be explained by the following reaction mechanism for oxygen introduction:



## STABILITY

Sulfur dyes have great affinity for oxygen, and this is as true during manufacture as during storage. All steps in the manufacture where the dye, or the incompletely formed dye, is in moist, solid form should be watched carefully for any undue rise in temperature which might cause a fire. The hot escaping hydrogen sulfide gas should always be conducted away through a long stack or condenser, and a hot charge of any sulfur dye must not be exposed to air without sufficient dilution of the supernatant surface with steam or inert gas. The apparatus used for sulfur-baking melts should be provided with steam or inert gas inlets.

Most sulfur dyes are stable if stored in airtight containers, although there are some colors which gradually undergo a change over a long period of time even though stored in the absence of air. The greens made from phenyl- and tolylnaphthylaminesulfonic acids combined with *p*-aminophenol, and the blue made from 4-hydroxy-2',4'-dinitrodiphenylamine, are among the dyes that gradually suffer a loss of color on long storage. The oxidation of sulfur dyes in powder form is believed to involve the formation of sulfur dioxide and trioxide, which in turn may cause further destruction of the dye molecule.

Sulfur Black (*C.I.* 978) made from dinitrophenol is stabilized with sodium sulfide (see p. 453), but even this is not a permanent protection. Prior to knowledge of the sodium sulfide stabilization method, this manufacture was accompanied by many fires, particularly in warehouse storage. Dye users were frequently plagued with fires which were almost certain to follow if a barrel of this dye was left open for several days. The hazard was of such a magnitude in the early period of the manufacture of this dye that the dry color was sometimes slaked with air by workmen who piled the dry powder in a heap and carefully watched the rise in temperature. As soon as the temperature rose to the burning point, the workmen quickly spread the pile to get a cooling effect, and frequently it was necessary to pack the dye in drums and close the lid to prevent the oxidation from getting out of control.

## TECHNICAL PROCESSES

The manufacture of sulfur dyes can be illustrated by three processes for the production of Sulfur Black, Sulfur Orange, and Hydron Blue. Sulfur Black, one of the largest selling dyes, accounting for more than 10,000,000 lb., represents a typical aqueous polysulfide reflux fusion. Sulfur Orange is made by a conventional sulfur-baking method. Hydron Blue illustrates the manufacture of an indophenol; it employs a polysulfide-butanol reflux fusion and a special desulfuration treatment. (See also refs. 1-3.)

**Sulfur Black (*C.I.* 978).**

*Conversion of 1-Chloro-2,4-dinitrobenzene to 2,4-Dinitrophenol.*

375 gal.	water
5,000 lb.	1-chloro-2,4-dinitrobenzene (m.p. +47.5°C.)
2,030 lb.	NaOH 100% used as 30% solution = 3% excess over theory
100 lb.	sulfuric acid, 40%

Three hundred and seventy-five gallons of water is placed in a 3,000-gal. steel reaction kettle and heated to 65°C. At this temperature 5,000 lb. of 1-chloro-2,4-dinitrobenzene is added from a scale tank, and the charge is heated to about 88°C. with stirring.

With the temperature held at 88-92°C., the 30% sodium hydroxide solution is slowly fed into the 1-chloro-2,4-dinitrobenzene suspension at a uniform rate, requiring approximately 8 hr. When

the addition is complete, the charge is held at 88–92°C. for 1 hr. longer to complete the reaction. The excess sodium hydroxide is neutralized with 40% sulfuric acid, using Brilliant Yellow paper as an indicator.

**Sulfuration Procedure.** Six thousand nine hundred and thirty-eight pounds of polysulfide, equivalent to 3,110 lb. of  $\text{Na}_2\text{S}$  100% and 3,828 lb. of sulfur, is weighed and blown into a 3,200-gal. brick-lined steel fusion kettle, and heated to 90–100°C. The hot dinitrophenolate charge is passed into the polysulfide at a rate rapid enough to maintain constant boiling. At the end of the addition, which requires between 3 and 4 hr., the charge will have a boiling point of about 108°C.

The charge is concentrated under atmospheric conditions at a uniform boil to a volume of 1,750 gal. in the course of 12 hr. Steam, hydrogen sulfide, and ammonia are allowed to escape through the stack over the roof. When the fusion is found to be completed, it is cooled to 70°C. with water on the coils, then diluted with condensate water to nearly the full capacity of the melt kettle, and finally blown to a precipitation kettle. The completion of the fusion is indicated by a spot test on filter paper of a sample of the dye precipitated by addition of dilute acid until the pH approaches 7. If the outrun is colorless, the fusion is complete; if orange, more sodium polysulfide is needed; and, if yellow, fusion is incomplete and should be continued.

**Precipitation and Filtration.** The completed melt is discharged into a 5,200-gal. steel precipitation kettle and diluted to 3,500 gal. with water. Introduction of air for precipitation of the dye is started at 35–40°C. and the temperature allowed to reach 50–55°C. Complete precipitation, requiring about 7 hr., is indicated by a spot on filter paper which should show a colorless or very faint green outrun. After cooling to 35–40°C., the charge is diluted to a volume of 4,500 gal.

The precipitated dye is filtered through a wooden filter press at about 40°C., and the presscake is blown with air for a very short time to discharge the mother liquor. The weight of the presscake is approximately 12,000 lb.

**Stabilization and Drying.** A 2,800-gal. steel pasting kettle is charged with about 200 gal. of condensate water and 1,500 lb. of 40%  $\text{Na}_2\text{S}$  solution. Then the filtered dye presscake is fed into the kettle simultaneously with 3,500 lb. of 40%  $\text{Na}_2\text{S}$  solution. The volume is made up with condensate water to 1,500 gal. and the contents mixed to a uniform paste, blown to rotary vacuum dryers, and dried under vacuum with 15 p.s.i. steam on the jacket and 60 p.s.i. on the shaft. The time required for drying is approximately 40 hr. After testing for dryness, the product is discharged. The weight of dried concentrated color is approximately 7,500 lb.

The dye is standardized to type by grinding and mixing with approximately 3,500 lb. of common salt and 500 lb. soda ash, giving approximately 11,500 lb. of Sulfur Black.

#### **Sulfur Orange (C.I. 948).**

##### *Sulfuration.*

225 lb.	toluene-2,4-diamine (tech.)
90 lb.	benzidine base (tech.)
900 lb.	sulfur

The sulfur is added to a Frederking pan and heated to 195°C. by circulating hot water at 225°C. Toluene-2,4-diamine and benzidine are then added in small portions at 190–195°C. As a precaution against the possible explosion of dry hydrogen sulfide gas on contact with air, steam is introduced over the fusion melt and is exhausted through the stack of the kettle. The charging door is closed and the space above the fusion melt is kept at 200°C. for 15 hr. After the 15 hr. of baking, the Frederking pan is cooled down and the porous brittle fusion is ground down by the agitator and discharged through the bottom outlet. Yield: approximately 990 lb.

##### *Desulfuration.*

550 lb.	100% NaOH as approx. 30% solution
200 lb.	sodium sulfide fused flakes, 60%
990 lb. (approx.)	sulfurated product

The ground sulfurated product is sifted into the 30% sodium hydroxide solution at 80°C. and then held at 105°C. for 4 hr. in any ordinary steel kettle. The sulfide flakes are added to the charge, and the volume is brought up to 450 gal. with water, and, when solution is complete, the hot charge is filtered to remove traces of insoluble matter. The filtrate and washings are run into a steam-jacketed pot for evaporation to a heavy paste, and finally dried on pans in an air dryer at 70–80°C. As the dried dye is very hygroscopic, it must be handled quickly during the subsequent standardization by

grinding and mixing with about 150 lb. of anhydrous sodium sulfate. Yield: 1,900 lb. of Sulfur Orange.

**Hydron Blue (C.I. 969).**

*Indophenol Intermediate.*

7,690 lb.	sulfuric acid 95%
330 lb.	<i>p</i> -nitrosophenol 100% as 88% dry cake
440 lb.	carbazole (tech.), 98% purity
24,750 lb.	water
9,900 lb.	ice
293 lb.	iron powder

Five thousand three hundred and thirty pounds of 95% sulfuric acid is charged into a 1,000-gal. steel, acid-brick-lined kettle and cooled to 0°C. with brine on coils and jacket. Then 440 lb. of carbazole is screened in during 2 hr. at 0°C. and stirring is continued for 2 hr. at this temperature. The temperature is allowed to rise to 3–5°C. with occasional stirring over the next 5–8 hr. and then lowered to –28°C.

Two thousand three hundred and sixty pounds of 95% sulfuric acid is charged into a second 1,500-gal. steel, acid-brick-lined kettle, and 330 lb. of 100% nitrosophenol as 88% dry cake is added in 2 hr. time at –5 to –10°C., after which the temperature is lowered to –28°C.

During agitation of the nitrosophenol solution, the carbazole solution is added over a period of 2–3 hr., maintaining a temperature of –20 to –23°C., and continuing agitation for 1 hr. longer.

While the condensation is in progress, 24,750 lb. water, 9,900 lb. ice, and 293 lb. iron powder are charged into a 6,000-gal. steel, acid-brick-lined kettle, and to this the finished indophenol condensation is added over a 1-hr. period, allowing the temperature to rise to 20–25°C. After agitation for 6 hr. the product is filtered and washed. The presscake is sludged in a 4,000-gal. steel, acid-brick-lined kettle and is refiltered and washed in the press until it is free of the acid and iron solution. The washed indophenol presscake is then dried over a drum dryer. Yield: 2,300 lb. presscake = 700 lb. dry indophenol.

*Sulfuration.*

	charge	= 5,700 lb. as 95%
5,700 lb. 95% butanol:	recovered	= <u>5,415 lb. as 95%</u>
	consumed	= 285 lb. as 95%

1,003 lb.	sodium sulfide flakes, 60%
1,267 lb.	sulfur
1,056 lb.	indophenol intermediate
700 lb.	sodium chloride for distillation
2,500 lb.	sodium chloride as a 15° Bé. solution for washing
242 lb.	sodium sulfide crystals, 30%
35 lb.	HCl concd. (35%)

The butanol, sulfide flakes, and sulfur are charged into a 3,250-gal. brick-lined, steel melt kettle equipped with steel condenser and heated at 60–70°C. for 2 hr. to form the polysulfide. After cooling to 30°C., the indophenol is added. The fusion is then brought to a boil and allowed to reflux for 36 hr. at a temperature of 107–109°C.

After completion of the reflux, the melt is cooled to 60°C. and the kettle is vented with steam to displace hydrogen sulfide gas. The charge is then diluted to 2,064 gal. with "water butanol" obtained from a previous batch, or else with condensate water. Then 700 lb. of sodium chloride is added, and the charge is heated to a boil with steam on the coil, and live steam is introduced under the surface of the charge to distill the butanol. The distillation is continued until a total of 1,800 gal. of distillate has been collected. The recovered butanol is separated from a water layer, dehydrated with potassium carbonate, and used over again with a certain amount of new butanol.

The melt is cooled to 70°C. and the volume adjusted to 1,732 gal. with condensate water. Two hundred and forty-two pounds of sodium sulfide crystals is added, and the charge is stirred for 1 hr. at 60–70°C. and then filtered through a wooden filter press, discarding the filtrate. The presscake is washed with a fresh solution of 15° Bé. sodium chloride solution until free of sodium sulfide.

*Desulfuration and Standardization.* Two thousand eight hundred gallons of fresh water and



234 lb. of sodium carbonate are charged into a steel kettle and stirred until the sodium carbonate is dissolved. The dye presscake is then added, and air is blown vigorously through the charge until the proper shade of dye has been obtained. The air-treated product is filtered through a wooden filter press. The presscake is ground in a rubber-lined ball mill and finally adjusted to type in a standardization kettle. The paste receives an addition of 3-4% of a thickener. Yield: 8,500 lb. Hydron Blue paste (equivalent to 2,640 lb. dry Hydron Blue powder).

## ECONOMICS

The importance of sulfur dyes can be gaged from Table II.

TABLE II. U.S. Sales of Sulfur Dyes—1953.

Dyes	Pounds	Av. price per lb., dollars	Total price, dollars
Blacks	9,251,000	0.21	1,979,000
Blues	4,036,000	0.36	1,471,000
Browns	4,145,000	0.28	1,146,000
Greens	1,932,000	0.59	1,146,000
Maroons (red, brown, and bordeaux)	406,000	0.75	306,000
Olives	177,000	0.49	86,000
Tans <sup>a</sup>	263,000	0.35	93,000
Yellows	441,000	0.37	163,000
All others	206,000	0.25	52,000
<i>Total dye (all types) sales</i>	<i>151,675,000</i>	<i>1.10</i>	<i>167,526,000</i>
<i>Total sulfur dye sales</i>	<i>20,594,000</i>	<i>0.31</i>	<i>6,349,000</i>

<sup>a</sup> Figures for tans are for 1951 and are not included in the 1953 total; all others taken from U.S. Tariff Commission, *Synthetic Organic Chemicals, U.S. Production and Sales 1953*.

Various trade names have been used by manufacturers or dealers to designate sulfur dyes sold by them, although some prefer to use simply the term "sulfur" to indicate this class of dyes. The more important designations or trade names used at present in the U.S. are:

Name	Manufacturer
Accosul (Acco)	Augusta Chemical Co.
Amalthion	John Campbell & Co.
Calcogene	American Cyanamid Co.
Eclipse	Geigy Co.
Faleo	Fallek Products Co., Inc.
Hydron	General Aniline
Immedial	General Aniline
Indocarbon	General Aniline
Katigen	General Aniline
Pyrogene	Ciba Co.
So-Dye-Co	Southern Dyestuff Corp.
So-Dye-Sul	Southern Dyestuff Corp.
Sulfindone	National Aniline
Sulfogene	Du Pont
Thional	Sandoz Chemical Works

## Bibliography

- (1) *BIOS Rept.* No. 983, p. 43.
- (2) *BIOS Rept.* No. 1155.
- (3) *FIAT Rept.* No. 1313, PB-85172, Vol. II, p. 304.

- (4) *FIAT Rept.* No. 1313, PB-85172, Vol. III, p. 228.
- (5) Fieser, L. F., and Fieser, M. A. P., *Organic Chemistry*, Reinhold, N.Y., 1950, p. 928.
- (6) Gilman, H. (ed.), *Organic Chemistry*, Wiley, N.Y., Vol. III, 1953, p. 352.
- (7) Jones, W. N., Jr., *J. Am. Chem. Soc.*, **54**, 4393 (1932).
- (8) Jones, W. N., Jr., *Chem. Revs.*, **36**, 291 (1945).
- (9) Karrer, P., *Organic Chemistry*, Elsevier, Houston, 1950, pp. 626, 629.
- (10) Lange, O., *Die Schwefelfarbstoffe, ihre Herstellung und Verwendung*, Spamer, Leipzig, 1925.
- (11) *Thorpe's Dictionary of Applied Chemistry*, Longmans Green, N.Y., Vol. XI, 1954, p. 245.
- (12) Venkataraman, K., *The Chemistry of Synthetic Dyes*, Academic Press, N.Y., Vol. II, 1952, p. 1059.
- (13) Zerweg, W., Ritter, H., and Schubert, M., *Angew. Chem.*, **60**, 141 (1948).

J. J. AYO, JR., AND ERNEST KUHN

**SULFUR HALIDES.** See *Sulfur compounds, inorganic.*

### SULFURIC ACID AND SULFUR TRIOXIDE

Properties.....	p. 460	Conversion.....	p. 484
Manufacture of sulfur dioxide.....	464	Absorption.....	480
Raw materials.....	464	Oleum production.....	490
Sulfur burners.....	466	Wet gas system.....	492
Ore burners.....	467	Special purpose plants.....	493
Other sources of sulfur dioxide.....	472	Economic aspects.....	494
Manufacture of sulfuric acid—chamber process.....	472	Analysis and specifications.....	496
Manufacture of sulfuric acid—contact process.....	478	Materials of construction and safety..	498
Wet gas purification.....	480	Uses.....	499
Hot gas purification.....	484	Bibliography.....	500
		Sulfur trioxide.....	501
		Bibliography.....	504

Sulfuric acid,  $\text{H}_2\text{SO}_4$ , formula weight 98.082, is a colorless, corrosive, oily liquid  $d_4^{25}$  1.8357, b.p.  $270^\circ\text{C}$ . It has always been considered the foundation of the inorganic chemical industry. Although some of its historic uses, such as the first step of the Leblanc process for manufacture of alkalies, have been superseded in whole, or in part, by development of other processes, it is being consumed in increasing volume in many new uses, such as the rayon industry, the titanium pigment industry, and in the petroleum industry, with the result that consumption of sulfuric acid in the U.S. has risen from about 4,200,000 net tons (that is, tons of 2,000 lb. of 100%  $\text{H}_2\text{SO}_4$ ) in 1935 to approximately 14,700,000 net tons in 1952. It is the widespread use of sulfuric acid throughout industry rather than tonnage that has caused consumption of sulfuric acid to be considered as a dependable barometer of general business conditions.

### History

**Chamber Process.** There is considerable doubt as to the date of discovery of sulfuric acid. Basil Valentine, in the latter part of the 15th century, described its preparation from calcined copperas and silica and also by burning sulfur with saltpeter (13); but there are indications that it had been produced at a much earlier date, perhaps as early as 1000 A.D. It was produced on a small laboratory scale by apothecaries during the early part of the 17th century by burning sulfur in moist air, and about a century later, on a somewhat larger scale, by burning a mixture of sulfur and saltpeter and condensing the acid formed in large glass vessels. In 1746 a lead chamber about 6 ft. square was built in Birmingham by Dr. Roebuck for burning a mixture of sulfur and saltpeter, thus forming the

basis for the chamber process which, with various modifications and on an ever-increasing scale, was employed exclusively for the manufacture of sulfuric acid until the latter part of the 19th century when the contact process was developed.

Steam was first employed in the chamber process in 1774, but it was about twenty years later before it was demonstrated that the saltpeter served only as an intermediary in the oxidation of the sulfur dioxide and that much niter could be saved by supplying the chambers with a continuous flow of air. All niter supplied to the chambers was lost in the exit gases until 1827 when the Gay-Lussac tower was first employed to recover the nitrogen oxides as nitrous vitriol (14). This was followed in 1859 by the invention of the Glover tower for denitrification of the nitrous vitriol, resulting in a great saving of niter. It will be noted that the development of the chamber process in its completed form took somewhat more than 110 years.

**Contact Process.** The contact process had its origin in the filing of a patent in 1831 by Peregrine Phillips, who recorded his discovery that sulfur dioxide could be caused to react directly with atmospheric oxygen by passage at strong yellow heat over platinum wire or finely divided platina. Many investigators followed up the method, but with no practical success, probably because their efforts were directed primarily toward development of a more economical substitute for the chamber process, since there was no great demand for fuming acid (oleum) for which the contact process was particularly adapted. This situation changed with the synthetic production of alizarin about 1870, and the realization that the future of the synthetic dye industry was dependent upon the availability of a cheap and plentiful supply of fuming acid. Up to that time, the relatively small demand for oleum had been met by the firm of Starek of Bohemia, who enjoyed a monopoly in distilling it from ferrous sulfate extracted from the Pilsen shales. With the publication of a paper by Clemens Winkler in 1875, great interest was awakened in the possibilities of the contact process. However, most investigators were misled by the faulty conclusions arrived at by Winkler, who insisted that the reaction could only be carried out by providing a stoichiometric mixture of two volumes of sulfur dioxide and one volume of oxygen. He prepared oleum by decomposing ordinary sulfuric acid by heat and, after removing the water vapor by condensation, passing the resultant dry sulfur dioxide and oxygen over platinized asbestos maintained at low red heat.

Winkler's process was employed by a number of firms, the earliest commercial production being by Emil Jacob at the Kreuznach Works, where the decomposition process was later replaced by production of sulfur dioxide from brimstone. Meanwhile, other German firms had returned to using pyrite burner gas as a source of sulfur dioxide, and a tremendous amount of time and money were expended in research, mostly directed to purification of the roaster gas to prevent contamination and poisoning of the catalyst. This culminated in Knietsch's classic lecture before the German Chemical Society in 1901 (5) revealing, in part, some of the many investigations that had been carried out by the Badische Anilin und Soda Fabrik during the years in which that firm's production at Ludwigshafen had increased from 18,500 tons (1888) to 116,000 tons (1900). In addition to Badische, patents were also taken out between 1898 and 1902 on the Mannheim process which employed a first stage of conversion utilizing a shaft filled with ferric oxide followed by a final stage employing platinum, the Schröder-Grillo process employing platinum-impregnated magnesium sulfate as catalyst, and the Tentelew Chemical Company process, which employed the principle of filtration and final washing with a dilute alkaline solution, thus utilizing a chemical purification process as contrasted with the Badische mechanical and physical procedures. Tentelew also introduced many novel features of apparatus design (7).

TABLE I. Density of Sulfuric Acid Solutions.

H <sub>2</sub> SO <sub>4</sub> , % by wt.	Sp.gr. <sup>15</sup>	H <sub>2</sub> SO <sub>4</sub> , % by wt.	Sp.gr. <sup>15</sup>	H <sub>2</sub> SO <sub>4</sub> , % by wt.	Sp.gr. <sup>15</sup>
5.0	1.0332	40.0	1.3065	75.0	1.6740
10.0	1.0681	45.0	1.3515	80.0	1.7323
15.0	1.1045	50.0	1.3990	85.0	1.7841
20.0	1.1424	55.0	1.4494	90.0	1.8198
25.0	1.1860	60.0	1.5024	95.0	1.8388
30.0	1.2220	65.0	1.5578	100.0	1.8357
35.0	1.2636	70.0	1.6151		

## Properties

**Sulfuric Acid 0–100%.** The *density* of sulfuric acid solutions is given in Table I (3). The density of sulfuric acid is often reported in degrees Baumé, according to the formula  $^{\circ}\text{Bé.} = 145 - (145/\text{sp.gr.})$ . Baumé and specific gravity values are given in Table II.

TABLE II. Baumé and Specific Gravity Values of Sulfuric Acid Solutions.

$^{\circ}\text{Bé.}$	Sp.gr. $_{60^{\circ}\text{F.}}^{60}$	% $\text{H}_2\text{SO}_4$	$^{\circ}\text{Bé.}$	Sp.gr. $_{60^{\circ}\text{F.}}^{60}$	% $\text{H}_2\text{SO}_4$
50	1.5263	62.18	58	1.6667	74.36
51	1.5426	63.66	59	1.6860	75.99
52	1.5591	65.13	60	1.7059	77.67
53	1.5761	66.63	61	1.7262	79.43
54	1.5934	68.13	62	1.7470	81.30
55	1.6111	69.65	63	1.7683	83.34
56	1.6292	71.17	64	1.7901	85.66
57	1.6477	72.75	65	1.8125	88.65
			66	1.8354	93.19

In Germany and France the Baumé scale is calculated using a modulus of 144.3 instead of 145, giving slightly different figures, which are, for the most frequently used values:

U.S. Bé.	German Bé.	% $\text{H}_2\text{SO}_4$
50	49.76	62.18
60	59.71	77.67
66	65.68	93.19

The total *vapor pressure* of aqueous solution of sulfuric acid at 100°C. and the partial pressures of  $\text{H}_2\text{SO}_4$  and  $\text{H}_2\text{O}$  over sulfuric acid solutions at varying temperatures are given in Table III and Table IV (11), respectively.

TABLE III. Total Vapor Pressure of Sulfuric Acid Solutions at 100°C.

% $\text{H}_2\text{SO}_4$	95	90	85	80	75	70	65	60	50	40	30	20	10
mm. Hg.	0.237	1.49	5.39	13.9	32	67	114	178	326	474	590	678	720

TABLE IV. Partial Pressures of Sulfuric Acid and Water over Sulfuric Acid Solutions.

89.25% $\text{H}_2\text{SO}_4$			95.06% $\text{H}_2\text{SO}_4$			98.00% $\text{H}_2\text{SO}_4$			99.23% $\text{H}_2\text{SO}_4$		
$^{\circ}\text{C.}$	$p_{\text{H}_2\text{SO}_4}$	$p_{\text{H}_2\text{O}}$	$^{\circ}\text{C.}$	$p_{\text{H}_2\text{SO}_4}$	$p_{\text{H}_2\text{O}}$	$^{\circ}\text{C.}$	$p_{\text{H}_2\text{SO}_4}$	$p_{\text{H}_2\text{O}}$	$^{\circ}\text{C.}$	$p_{\text{H}_2\text{SO}_4}$	$p_{\text{H}_2\text{O}}$
183.0	0.5	78.8	180.0	2.1	10.1	204.0	5.9	0.0	211	33.2	
197.5	1.3	116.9	200.0	4.8	21.2	218.5	9.8	1.5	225	49.9	
216.5	2.1	233.1	215.5	8.5	46.5	234.5	14.7	3.2	227	55.4	
230.0	3.6	306.3	232.0	13.4	91.9	249.0	28.5	2.6	244	84.1	< 0.1
241.5	5.3	414.8	244.5	19.9	120.1	261.0	38.8	5.0	261	163.8	
			261.0	27.9	180.7	273.0	61.9	5.3	270	229.8	
			270.0	39.9	254.9	285.0	91.6	11.8	281	272.3	
			282.0	52.6	350.2	295.0	132.3	14.7	290	381.5	

In the system  $\text{H}_2\text{SO}_4\text{-H}_2\text{O}$  there is a constant-boiling mixture at 98.3%  $\text{H}_2\text{SO}_4$ .

Many determinations of the *specific heat* of sulfuric acid solutions have been made, and it is believed that the most accurate are those given in Perry (11) and in ref. (12), which are shown as Figure 1. The *boiling point* curve of Figure 2 is that presented by Zeisberg (15) and the *freezing point* curve of Figure 2, the *viscosity* curve of Figure 3 and the *index of refraction* curve of Figure 3 are derived from data presented in Mellor (6). The *electrical conductivity* curve of Figure 4 is plotted from data of

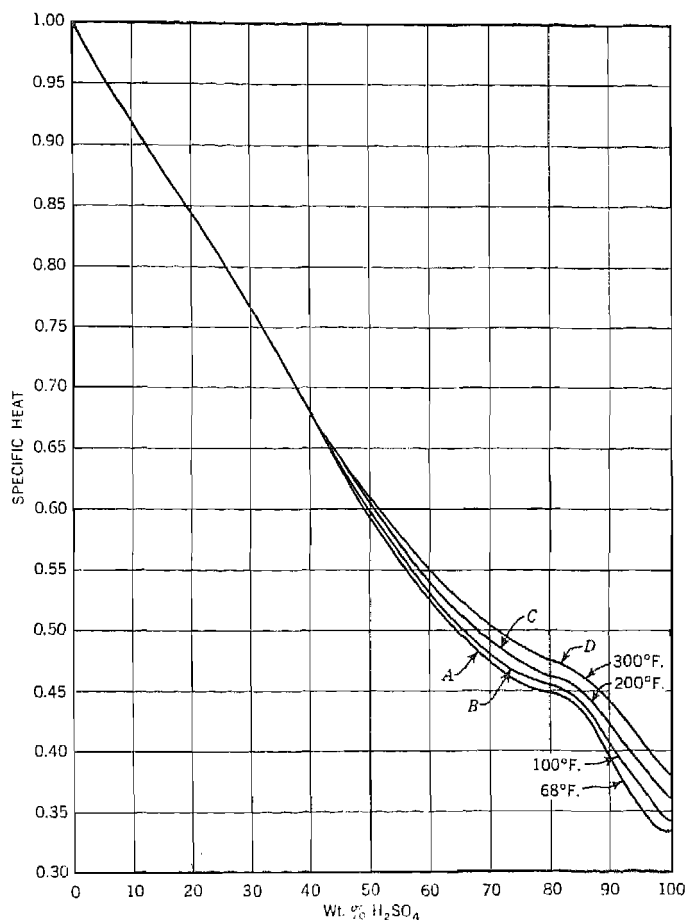


Fig. 1. Specific heat of sulfuric acid solutions.

Kohlrausch and the *heat of dilution curve* of Figure 4 from National Bureau of Standards data.

**Oleum.** Fuming sulfuric acid or oleum consists of a solution of sulfur trioxide in 100% sulfuric acid (which is often referred to as monohydrate, since it comprises  $\text{SO}_3$  combined with one molecule of water). The strength of oleum is designated as per cent by weight of free sulfur trioxide: thus 20% oleum contains 20%  $\text{SO}_3$  and 80%  $\text{H}_2\text{SO}_4$  by weight. Since the physical properties of oleum are quite different from those of sulfuric acid, they are presented independently. Some of the values most in dispute are those covering specific heat, vapor pressure, and freezing point. The data on

*density* presented in the 1901 lecture of Knietzsch (5) are generally considered too high, and this is attributed to the fact that the determinations were probably on Nordhausen acid of questionable purity. Table V presents data of the General Chemical Division, Allied Chemical & Dye Corp.

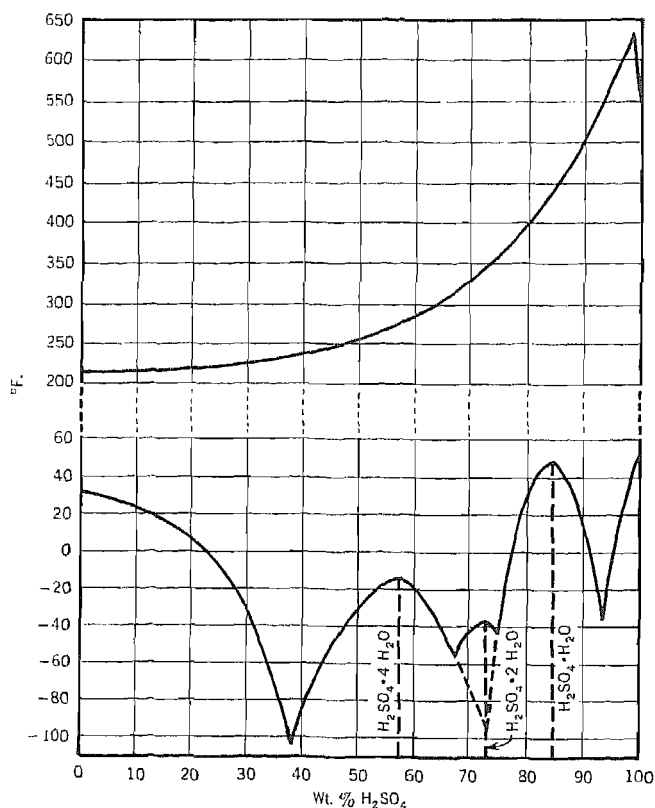


Fig. 2. Boiling and freezing points of sulfuric acid solutions.

TABLE V. Density of Oleum.

SO <sub>3</sub>	% by weight H <sub>2</sub> SO <sub>4</sub>	Total SO <sub>3</sub>	Equivalent H <sub>2</sub> SO <sub>4</sub> , %	Density (15° C.)
10	90	83.47	102.25	1.8716
20	80	85.31	104.50	1.9056
30	70	87.14	106.75	1.9412
40	60	88.98	109.00	1.9737
50	50	90.82	111.25	1.9900
60	40	92.65	113.50	1.9919
65	35	93.57	114.63	1.9842

The most accurate data on the *vapor pressure* of oleum are given by Miles, Niblock, and Wilson (9), from whose data Figure 5 was made, showing the equilibrium partial pressure of sulfur trioxide over oleum of various strengths at various temperatures.

The *boiling point* curve of Figure 6 was calculated from the same data (9) and is compared with prior data from Knietzsch (5) with which it is in reasonably close agree-

ment. The lower curve of Figure 6, which has been adopted by the Manufacturing Chemists Association of the U.S., is believed to represent the best available data on

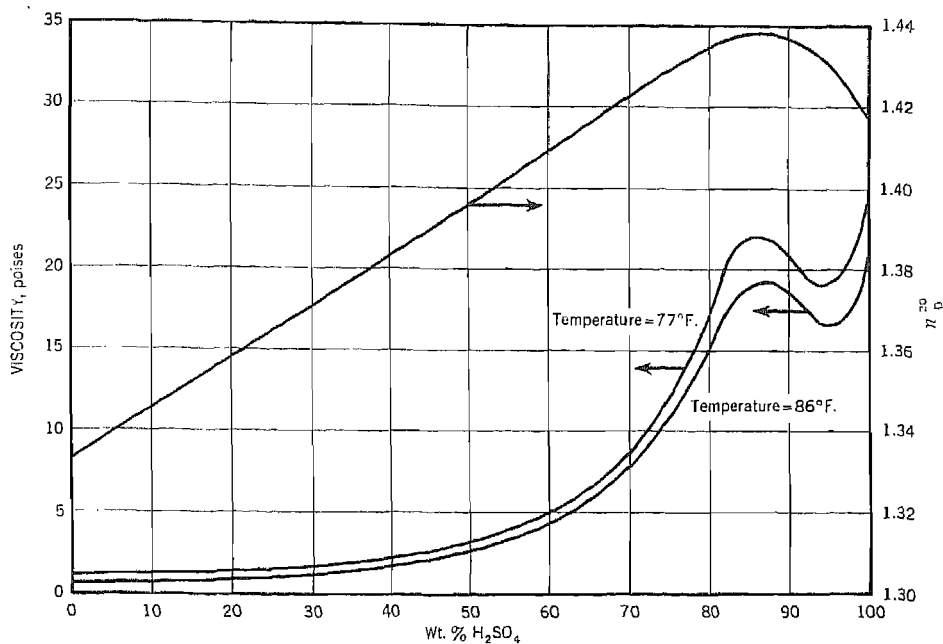


Fig. 3. Index of refraction and viscosity of sulfuric acid solutions.

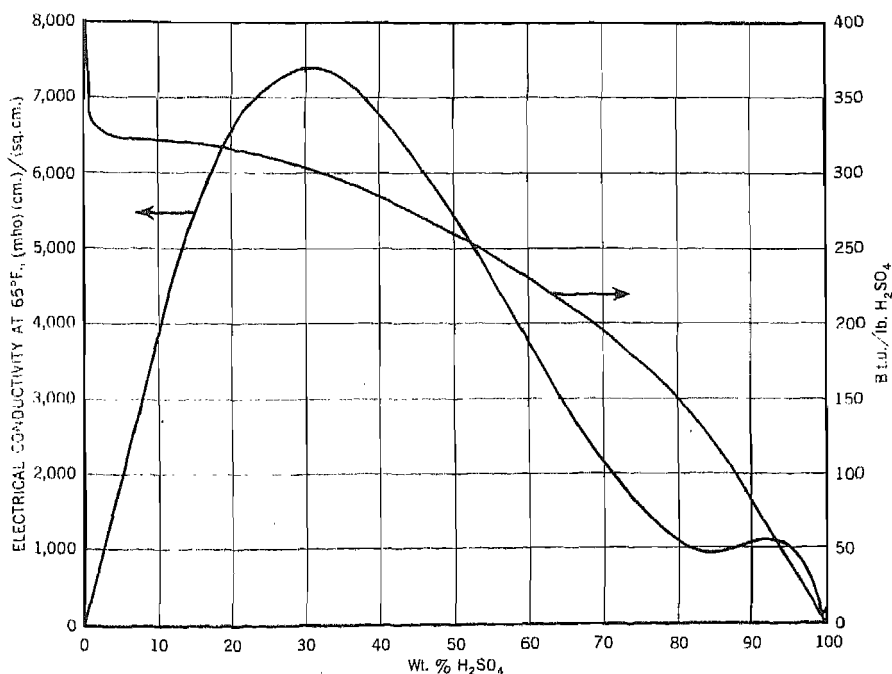
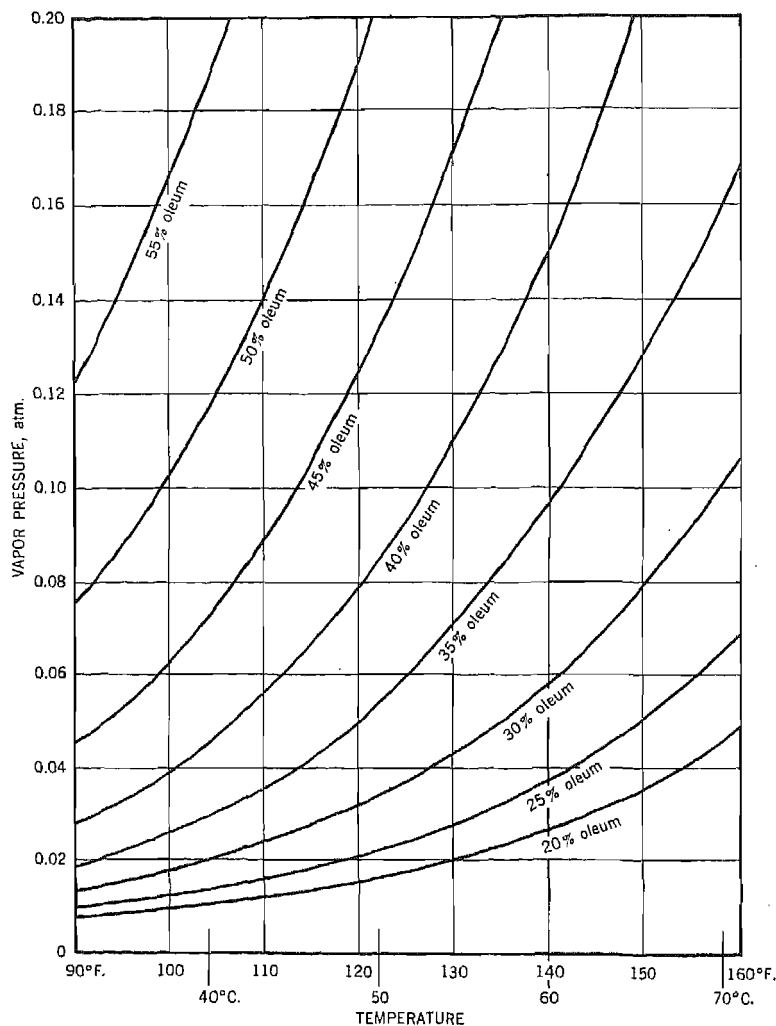


Fig. 4. Electrical conductivity of sulfuric acid solutions, and heat evolved on adding water to 1 lb.  $H_2SO_4$  (wt. % of resulting solution, at 77°F., read on abscissa).

freezing points. The *specific heat* curve of Figure 7 represents a portion of a curve presented by Miles, Niblock, and Smith (8), recalculated from total  $\text{SO}_3$  as presented by the authors to per cent oleum or free  $\text{SO}_3$ . The *viscosity* curve of Figure 7 is obtained



Courtesy General Chemical Division, Allied Chemical & Dye Corporation.

Fig. 5. Vapor pressure of oleum.

from Mellor (6). The *electrical conductivity* curve of Figure 8 is from the data presented by Kohlrausch and the *heat of solution* of gaseous sulfur trioxide in oleum (Figure 8) is plotted from data from several sources. See also p. 502. It is of interest to note here that the peaks on the density, freezing point, and viscosity curves correspond approximately with the composition of *pyrosulfuric acid*,  $\text{H}_2\text{S}_2\text{O}_7$ .

## Manufacture of Sulfur Dioxide

### RAW MATERIALS

The more important raw materials are *sulfur* (*q.v.*) and various metal *sulfides*.



The important metal sulfides are those of iron (pyrite,  $\text{FeS}_2$ , and pyrrhotite, approximately  $\text{FeS}$ ) and zinc,  $\text{ZnS}$ . Spain was originally the chief source of supply of pyrite, but there are large deposits in almost every country, although few are

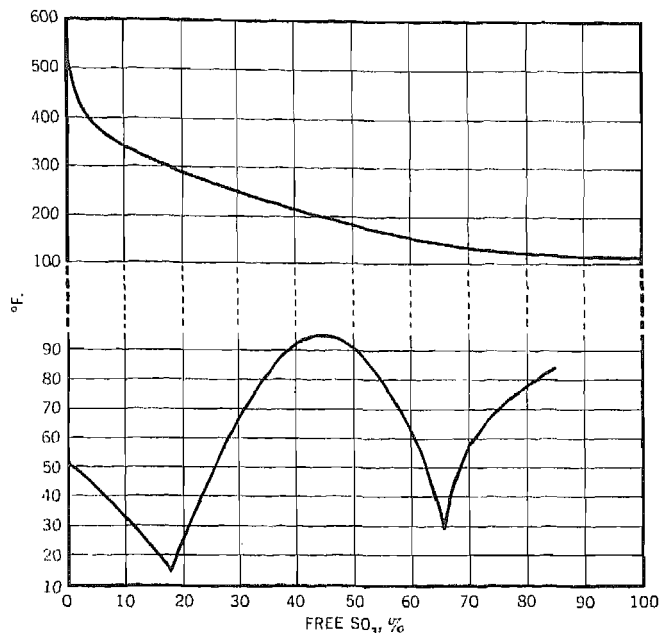


Fig. 6. Boiling and freezing points of oleum.

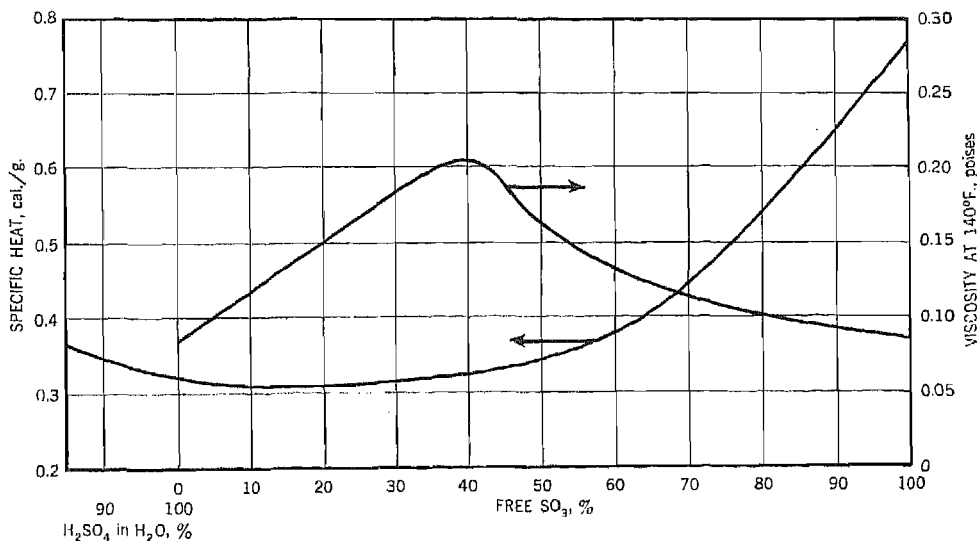


Fig. 7. Specific heat and viscosity of oleum.

worked owing to economic considerations. A large percentage of present U.S. consumption is imported from Canada, where it is a by-product of the selective flotation of ores that are mined for their nonferrous values. Pyrite also occurs as veins in coal

deposits, but these "coal brasses" contain so much carbon that they are not favorable for acid manufacture unless the carbon content is materially reduced, and the cost of this beneficiation is excessive. Large deposits of pyrrhotite exist in the eastern part of the United States and some of these deposits are worked for acid manufacture, although the sulfur content of pyrrhotite is approximately 70% that of pyrite. Zinc sulfide, sphalerite,  $\text{ZnS}$ , is roasted to convert it to zinc oxide, and the by-product sulfur dioxide gas is used for manufacture of acid. Of the several metal sulfides, only pyrite and pyrrhotite are mined expressly for acid manufacture. See *Iron compounds*;

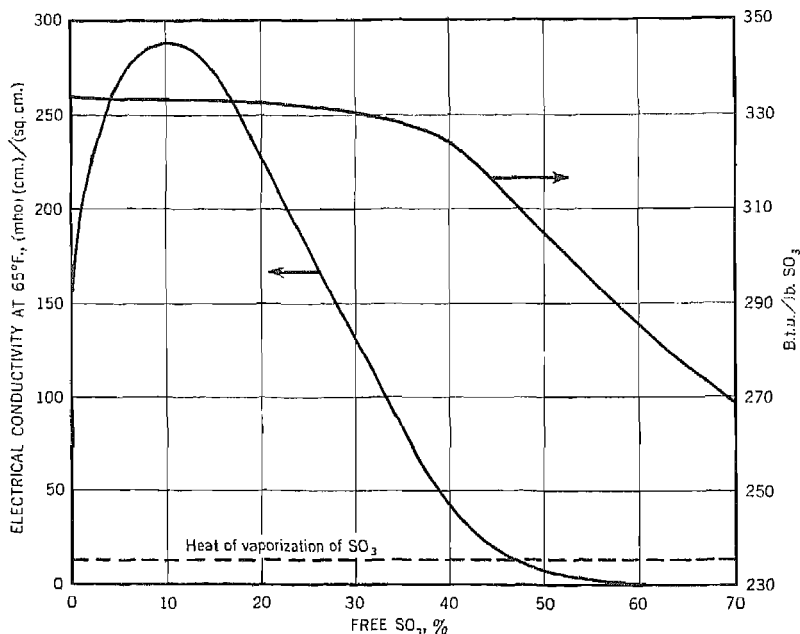


Fig. 8. Electrical conductivity of oleum, and heat evolved on adding  $\text{H}_2\text{SO}_4$  to gaseous  $\text{SO}_3$  (% free  $\text{SO}_3$  of resulting oleum, at  $86^\circ\text{F}$ ., read on abscissa).

**Zinc.** Since about 1936, hydrogen sulfide (see *Sulfur compounds, inorganic*) recovered from "sour" natural gas and oil refinery still gases has been used in production of sulfuric acid in ever-increasing amounts at a number of locations. As in the case of the smelter gas, this was initiated as a means of avoiding damage to vegetation and atmospheric pollution.

#### SULFUR BURNERS

**Masonry Burner.** The earliest sulfur burners employed in conjunction with the lead chamber process consisted of a brick chamber with brick arch, containing a horizontal cast iron pan with a low upstand on which the sulfur was charged intermittently. Impurities in the sulfur formed a scum on the surface of the molten sulfur that required occasional raking to secure relatively uniform gas. The ash was periodically scraped over the front upstand, which was set at an angle of  $30$  to  $45^\circ$ . Niter "hogs" (p. 474), used in conjunction with the chamber process, were installed in an extension of the brick chamber in which combustion of any vaporized sulfur was com-

pleted. Frequently the top arch supported paus in which some concentration of the chamber acid was accomplished.

**Glens Falls Burner.** Although many improved burners were employed in subsequent years, the most popular developed was the Tromblee and Paull, commonly known as the Glens Falls burner, and many of these are still in use. They consist of an unlined horizontal cylindrical steel shell with conical ends mounted on trunnions and revolved at about 2 r.p.m. Angle irons are sometimes attached to the shell to increase the rate of burning and to break up dirt accumulations. Sulfur is fed to one end through a helicoid conveyor and the cone at the opposite end terminates in a flange that is spaced relatively close to a similar flange on the nozzle of a combustion chamber. The burner operates under a negative gage pressure.

**Vesuvius Burner.** Another burner that has been used to some extent in the past, that of Hinzke, is commonly known as the Vesuvius burner. This is a vertical cylindrical steel shell lined with firebrick, the arch of which supports a sulfur melting kettle, the molten sulfur dropping through the burner over a series of superimposed cast iron shelves. The gas, which contains both sulfur dioxide and sulfur vapor, is passed through a separate combustion chamber to which additional air is admitted to complete combustion.

**Sublimer.** All of the above burners are in fact part sublimers and part burners, the relative proportion depending on radiation characteristics. Another unit employed extensively is known as a sublimer, since in operation the combustion occurring is only that necessary to maintain an operating temperature of about 700°F. This unit can be regulated to provide a gas of very uniform sulfur dioxide concentration by controlling the volume of air that is bubbled through the molten sulfur. Less than 10% of the sulfur is burned to sulfur dioxide, the remainder passing over as vapor to the combustion chamber, where additional air is admitted. This unit is suitable for operation at positive gage and can be supplied with dry (solid) sulfur, although the preferred practice is to melt the sulfur and either filter it or allow impurities to settle.

**Molten Sulfur Spray.** The most recent practice involves spraying the settled or filtered molten sulfur directly into the combustion chamber, where the necessary air is admitted. This method also is applicable to plus-pressure operation. In any procedure involving the handling of molten sulfur, the lines and spray nozzles must be steam-jacketed and a pressure employed that will hold the molten sulfur within approximately 275 to 310°F., where its viscosity is at a minimum. Above 320°F. the viscosity rises sharply, and at 390°F., for example, is 3000 times that at 300°F.

## ORE BURNERS

**Lump Burners.** The earliest pyrite burners were known as lump burners because the ore was charged to burners in lumps  $2\frac{1}{2}$  to 3 in. in size. Jaw crushers were employed to some extent, but the preferred method was hand breaking of the coarse ore because much less fines was produced. These burners of 24–30 sq.ft. area, were built in sets of 36 to 48 burners, erected in a double row back to back. Ore was charged by hand onto the bed, supported on grate bars. The ore charge approximated 15 lb./sq.ft. grate area per 12 hr., and charging time on individual burners was staggered so that fresh ore was being charged to some burner about every 15–20 min. in order to secure uniform gas for the acid plant. It is extremely doubtful whether any lump burners are in operation today, at least in the U.S. The cinder usually contained from 3–5% sulfur.

**McDougall Burner.** The earliest mechanical burner was the McDougall, which consisted of 6-ft. diameter cast-iron flanged rings bolted together in a vertical pile to provide seven superimposed firebrick hearths, each of which was supported from a bearing ring at the flange. This burner never attained commercial importance, but the basic principle was employed in the highly successful Herreshoff and Wedge burners.

**Herreshoff Furnace.** The Herreshoff furnace, in its improved form, consists of a steel cylindrical vessel of varying diameter, lined with firebrick and containing seven or more internal brick hearths, plus the top hearth which is employed as an ore dryer. Arms, which may be either steel or cast iron, are connected to an air-cooled central cast iron shaft containing passages whereby the cooling air is circulated through the arms as well as shaft. The shaft is supported on a button-bearing at the base and revolved at approximately  $\frac{1}{2}$  r.p.m. The arms, which are oriented  $90^\circ$  at adjacent shelves, are fitted with cast-iron rabblers that move the ore inward on one hearth and outward on the next hearth. The rabble blades are bent so that the burning ore is turned over as well as advanced. Hot air leaving the shaft is passed through a horizontal duct to an annular bustle pipe by which the air can be delivered to a series of small vertical cast iron flues of rectangular shape that are set flush with the interior of the brick lining. These temperature control flues serve the double purpose of transferring heat from the very hot hearths (second and third from the top) to the lower hearths and delivering the heated air to the bottom hearth, thereby assisting in the desulfurization of the cinder. A seven-hearth 15 ft.-9 in. diameter burner of this type is capable of roasting 10 net tons per day of ordinary pyrite containing 48–50% sulfur provided ore is crushed to  $\frac{3}{8}$ -in. size. The cinder ranges from 1 to 4% sulfur, depending on the character of the ore. Particles larger than  $\frac{3}{8}$  in. are likely to have an unburned core of green ore.

**Wedge Furnace.** The Wedge furnace (see Vol. 4, p. 400) follows the same general principle, but is somewhat larger in size and is characterized by the use of a large 5-ft. diameter central shaft constructed of steel, open at the top and bottom, and protected from the furnace gases by a firebrick facing which eliminates the need of cooling. The arms are water-cooled, with a separate control to each arm, and are keyed in place from inside the shaft, so that, owing to the large shaft diameter and the insulation, workmen can enter the shaft to replace arms or carry out other repairs without shutting down and cooling off the furnace. The large Wedge furnaces are stated to have a capacity of 20 net tons per day of normal pyrite. They have reportedly been used with good success in the roasting of lead matte containing about 25% sulfur.

**Hegeler Furnace.** The Hegeler furnace was installed for roasting zinc blende. This mechanical furnace, which is 75 ft. long, is constructed of brick and divided by a central wall into two compartments, each containing seven shelves, the lower two being built with muffles to permit use of fuel to assist in desulfurization of the ore. Agitation of the bed is accomplished by dragging a rake fitted with rabblers through a hearth by means of a rod. The rake is then removed through a large door, permitted to cool off, and then started back over the adjacent shelf. Such a furnace can handle only about 40 tons of blende per 24 hr. and the cost of operating labor and fuel is very high. Since the rabbling is of an intermittent nature, desulfurization is not very good and the gas produced is only about 4 to 5%  $\text{SO}_2$ , which imposes quite a penalty on the associated acid plant.

**Flash Roaster.** Application of selective flotation procedures for recovery of values from ores necessitated very fine grinding, the particle size in many cases being

reduced to 300 mesh and even finer, and as the tailings consisted of a mixture of pyrite and gangue, a final flotation permitted recovery of the pyrite at relatively low cost. Although this material created problems in operation of the mechanical roasters due to more rapid combustion, it was particularly well suited for flash roasting. This resulted in the development of an entirely new type of roaster in which the ore was burned while in gaseous suspension, as contrasted with the predominantly bed roasting carried out in the mechanical burners.

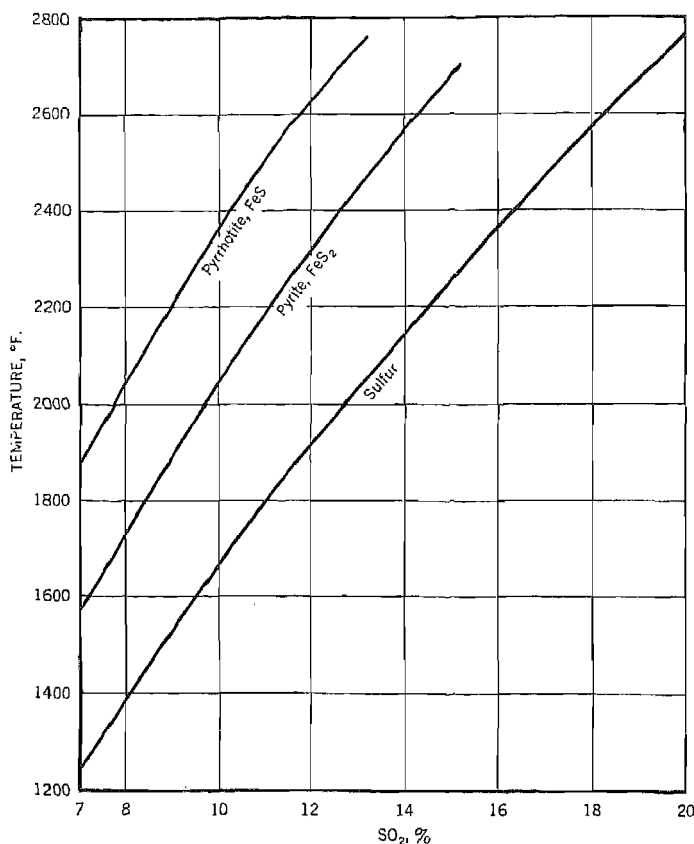
From an initial plant installation in 1926 of such a burner of approximately 900 cu.ft. capacity, successive installations of increasing size have been made, the most recent providing 20,000 cu.ft. of combustion space. The burner is a vertical steel vessel lined with refractory and fitted with a dome top and a conical or pyramidal base for discharge of cinder, but containing no moving parts. The principle has been employed in several different ways: the ore and combustion air may be admitted through the top arch with cinder discharged at the base and gas discharged through a side opening adjacent to the base; the ore may be fed to the burner through side injectors located just above the base with the remainder of the combustion air admitted to the base, and the gas outlet through a side opening just below the top arch; and a combination coflow, counterflow arrangement in which the ore is admitted with part of the combustion air through the top arch and the remainder of the combustion air admitted at the base, and the cinder discharged at the base, the side gas outlet port being just below the top arch.

When bottom injectors are employed, they must be mounted at an angle and the air pressure kept below the point where particles would strike either the top arch or the side wall, and when ore is introduced at the top, a nozzle design must be employed that will provide good dispersion over the cross-sectional area of the burner, securing rapid ignition, yet avoiding impingement on side walls. As desulfurization of the ore proceeds, a mixture of iron sulfide and oxide is reached that has a much lower fusion point than either, and, while the burning ore is in this sticky stage, impingement on any portion of the interior must be prevented to avoid the building up of a clinker.

The flash roaster possesses many advantages over the mechanical roaster from the point of view of sulfuric acid manufacture (apart from metallurgical considerations), the sole disadvantage being the cost of grinding the ore in the event that flotation concentrates are not available, and a heavier carry-over of fine cinder to the dust collectors. The advantages are: (a) combustion space about 10% of a Herreshoff or Wedge; (b) minimum repairs, since the burner contains no shaft, arms, or rables, resulting in substantially continuous operation; (c) high gas concentration, 11.5 to 12.0% on pyrite and 10% on pyrrhotite, permitting about 25% reduction in gas purification equipment; (d) increased credit for by-product steam when the gases from the burner are passed through a waste heat boiler; and (e) reduced formation of sulfur trioxide due to the high concentration and temperature of the gas and the rapid cooling of the gas through the conversion range when a waste heat boiler is employed. Sulfur trioxide would form a mist which would cause serious corrosion (sulfation), and it must be removed as a weak impure acid which is difficult to dispose of.

The theoretical temperature produced by the combustion of sulfur and iron sulfides is shown in Figure 9. The gas leaving the Herreshoff burner is at somewhat less than 1000°F., because of radiation loss and because the shaft and arms are air-cooled, and the cost of recovering heat in a waste heat boiler is difficult to justify. In the suspension roaster, the gas leaving is between 1750° and 1800°F. Moreover, this temperature is

maintained by the recycling of gas from the outlet of the boiler to prevent a temperature rise that would result in fusion of the cinder. On large well-insulated burners this recycled gas will range from 40 to 50%, the latter on pyrrhotite ore, where a higher temperature is reached due to oxidation of the larger quantity of iron. The temperatures



*Courtesy General Chemical Division, Allied Chemical & Dye Corporation.*

**Fig. 9. Temperature of sulfur dioxide gases from sulfur and iron sulfides.** Assumptions: combustion air, 95°F. (sulfur); 60°F. and 75% r.h. (sulfides); all sulfur burned to sulfur dioxide, all cinder burned to  $\text{Fe}_3\text{O}_4$  at combustion temp. Pyrite 48.0% sulfur, cinder to ore ratio 68%, pyrrhotite 32.5% sulfur, cinder to ore ratio 87.3%.

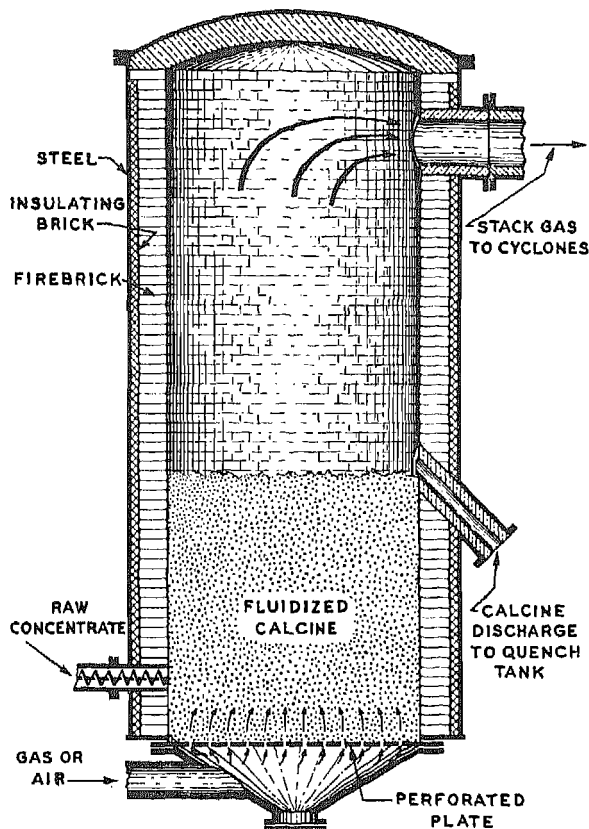
referred to above are those of the gases produced, as the ore particles on flashing are raised to incandescence, thus tending to form ferrites, and the cinder will be found under the microscope to consist of minute hollow spheres that have obviously been raised above the melting point. The interior of a burner operating on pyrite or pyrrhotite will be filled with luminous particles shooting about in all directions, but, where this type of roasting has been applied to zinc concentrates, no incandescent particles can be observed. The cinder from pyrite, pyrrhotite, or zinc blende contains 1.0–3.5% sulfur.

In addition to burners specifically designed for suspension roasting, many Herreshoff and Wedge burners have been converted to suspension roasting by removal of

shaft, arms, and internal shelves and quite satisfactory operation has resulted, with the result that the mechanical burner, as such, is becoming obsolete in operations specifically intended for sulfuric acid manufacture, although it still has metallurgical uses.

All of the burners described above are of such design that they must be operated under negative pressure.

**Fluidized Burner.** In recent years a new type of burner has been introduced in which a bed of comparatively fine ore, about 20–40 in. in depth when at rest, is



*Courtesy The Dorr Company.*

**Fig. 10. FluoSolids roaster.**

kept in motion by the upward flow of the combustion air, with result that the bed, while in motion, is increased to a depth ranging from 30 to 60 in. This type of burner takes the form of a tank, lined with firebrick and containing a perforated false bottom on which ore is carried and through which the oxidizing air is directed upward (Fig. 10). These burners are equipped with an overflow standpipe for discharge of cinders, but a very large percentage of the cinder is carried off mechanically in the gas stream, and with very fine ore the air pressure may have to be reduced to maintain the desired depth of bed. Since lack of agitation will cause the formation of a clinker, it is essential that the entire bed be kept in motion, and control of temperature is essential to avoid fusion. This control is effected by vaporization of water or utilization of heat

exchange means embedded in the ore bed, and many details remain to be worked out. The fluidized burner has advantages in certain metallurgical operations, but as of 1954 it is not certain whether it possesses any advantages over the flash roaster (from the point of view of sulfuric acid manufacture) other than the ability to handle a clump ore, and a coarser ore similar to that handled in the mechanical burners, whereas for successful operation of the flash roaster the particle size should be less than 60 mesh.

**Rotary burners and spray burners** are extensively used abroad, and in producing sulfur dioxide for other purposes than the manufacture of sulfuric acid and for some special plants (see p. 493). See "Sulfur Dioxide" under *Sulfur compounds, inorganic*.

**By-product Iron Oxide.** The iron oxide by-product resulting from the roasting of pyrite and pyrrhotite is marketable to blast furnace operators and provides a substantial credit against cost of manufacturing acid. To be acceptable, however, the roasted cinder must be subjected to a further processing to reduce sulfur content not to exceed 0.10% and effect agglomeration of the small particles. This can be accomplished in a rotary "nodulizing" kiln or in a sintering machine of standard design. Cinder containing zinc is unacceptable, but most other nonferrous constituents are not present in sufficient amount to be objectionable. The recently developed method of using taconite (see *Iron*) by furnacing pelletized iron oxide in an open shaft furnace also offers promise for beneficiation of the roasted cinder.

#### OTHER SOURCES OF SULFUR DIOXIDE

Hydrogen sulfide, as recovered from sour natural gas and cracking-still gases of oil refineries, can be burned as readily as natural gas, but the toxic properties require that very special precautions be observed in handling the gas. A serious disadvantage in its use for acid manufacture is the large amount of oxygen consumed in burning the hydrogen, the result being that, when adequate oxygen for conversion to sulfur trioxide is present, the concentration of sulfur dioxide is only two-thirds of that produced from brimstone. This results in a considerably larger plant investment.

Sulfur dioxide is a common by-product of many metallurgical operations. Large tonnages of sulfuric acid are produced from the gases from the smelting of sulfide ores. See such articles as *Copper*; *Zinc*. These smelter gases are suitable for both the chamber and contact processes, subject to limitations imposed by concentration and impurity content and gas purification requirements. Sulfur dioxide from gypsum, anhydrite, and other sulfates is used to manufacture sulfuric acid in Europe.

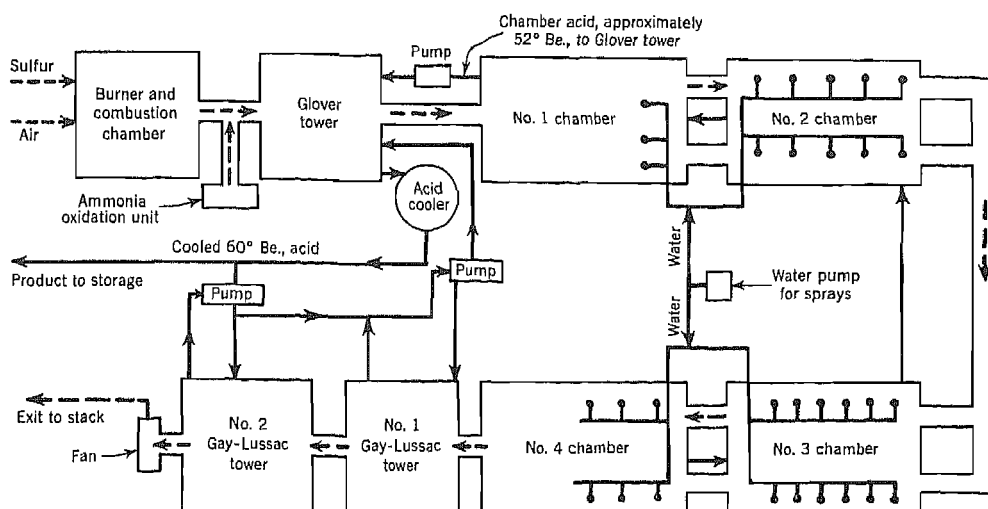
#### Manufacture of Sulfuric Acid—Chamber Process

Originally the chamber process employed sulfur dioxide gas produced from sulfur, but roaster gas or smelter gas was substituted later. As finally developed, the process employs the following principal units to which must be added the necessary accessories such as conveyors, pumps, etc. (see Fig. 11): (a) The Glover tower receives the hot burner gas, and is fed at the top with the nitrous vitriol from the Gay-Lussac tower, and with 52°Bé. (65%) acid from the chambers. Its functions are: to denitrify the Gay-Lussac acid, thus reducing niter requirements to a small make-up for process loss; to evaporate water from the chamber acid, thus concentrating it to about 60°Bé. (78%); cooling the gas to the point at which it can be safely introduced into the lead chambers; and supplying water vapor, equivalent to about one-third of the water requirement of the set (when producing acid of 52°Bé.). (b) A series of large lead



chambers, usually comprising from three to as many as ten, in which the reactions between sulfur dioxide, oxygen from the air, oxides of nitrogen, and water are carried out with resultant production of chamber acid. (c) Usually two Gay-Lussac towers in series, in which the oxides of nitrogen leaving the final chamber are absorbed in sulfuric acid of about 60°Bé. forming nitrous vitriol. (d) An ejector or fan to provide the necessary flow of air through the system. The ejector may be located in the exit stack from the Gay-Lussac tower, or a fan is usually placed between the final chamber and Gay-Lussac tower (occasionally between the Glover tower and first chamber, although this location is not preferred owing to the higher temperature at that point).

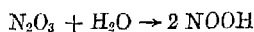
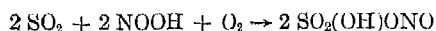
**Chamber Reactions.** Although the various reactions that may take place in the chambers have been the subject of endless arguments, the primary reactions are the formation of an intermediate compound, nitrososulfuric acid, from sulfur dioxide,



*Courtesy General Chemical Division, Allied Chemical & Dye Corporation.*

Fig. 11. Original chamber process.

nitrogen oxides, and oxygen, followed by its decomposition by water into sulfuric acid with liberation of nitrogen trioxide for continuation of the cyclic reaction according to the following equations:



In the conventional chamber set as described, it was the practice to provide about 16 cu.ft. of chamber space per pound of sulfur burned per 24 hr. and, while this space requirement could be somewhat reduced by more intensive working, this was generally not considered economical due to the additional loss of niter caused thereby.

For proper working of the process, it is essential that the gases leaving the final chamber be substantially free of sulfur dioxide, but contain not less than 5% free oxygen. A large glass bell jar, usually located in the flue at the exit of the final chamber, permits visual observation of the completeness of the reaction. Under normal conditions this glass would be filled with a characteristic clear ruddy or orange-red vapor, whereas if, through deficiency of niter, oxygen, or excess water, the oxidation of the

sulfur dioxide is incomplete, this glass takes on a cloudy yellow cast. In the presence of sulfur dioxide, the nitrogen oxides cannot be recovered in the Gay-Lussac tower. When this occurs, it is necessary to increase sharply the niter charge to restore proper conditions in the chambers.

**Glover Tower.** The Glover tower, as originally introduced, was a square lead vessel about 25 ft. high and of sufficient cross section to provide about 0.25 cu.ft./lb. of sulfur per 24 hr., or roughly 1.5% of the cubic contents of the entire chamber set. The bottom and the lower half of the sides were constructed of very heavy lead, about 35 lb./sq.ft., with the upper half of the sides about half this weight. The bottom and lower sides were lined with a temperature- and acid-resisting material, such as chemical stoneware 10 to 12 in. in thickness, and this was reduced to about half for the upper sides. The tower was erected within a frame consisting of vertical steel corner angles with horizontal members to support the sides. The top was of lighter lead (8–10 lb.) supported from above. The tower was packed with material similar to the lining, and acid distribution was secured by providing a central leaden box with overflow lips or pipes feeding from 30 to 40 separate compartments, each of which was connected by pipes to the top of the tower to effect a relatively uniform distribution of acid over the tower cross section. Later, round towers came into use and acid-proof stoneware in many manufactured forms was employed as packing.

The niter loss is frequently made up by supplying the Glover tower with spent nitric acid from other operations, or sodium nitrate can be potted with sulfuric acid in a cast iron "niter hog" located at the back end of the sulfur burner, or in more modern practice, by inclusion of a small ammonia-oxidation unit.

**Lead Chambers.** These vary in number, and in length from 50 to 200 ft., but they are usually restricted to a width of about 25 ft. and height of 20 ft. It is customary to erect the chambers some 10–12 ft. above grade to provide good air circulation. Each chamber consists of a bottom or pan of about 12 lb. lead, bent up at the edges, like a tray, to a height of about 2 ft. The chamber sides are of 6–8 lb. lead, supported from a steel or wood skeleton. Lead straps burned to the sheets are attached to this frame, and the lower ends of the sheets hang down in the 10–12 in. pool of acid carried in the pan, thus providing a gas-tight lute. The chamber top, also of light lead, is supported by lead straps burned to the horizontal top and attached to wood joists or steel members spanning the chamber width.

Small lead trays are placed inside the chambers to provide a continuous sample of the acid being produced. Thermometers are placed at one or more locations in each chamber, and the temperature and strength of the drip are used by the operator to control the working of the set, and to regulate the water supply to the chamber sprays.

The total water requirement of the chambers when producing 52°Bé. acid is approximately 2.25 lb. H<sub>2</sub>O per pound of sulfur burned. The Glover tower supplies about a third of this total, which may be sufficient for the first chamber, depending on the size and number of chambers in the set. The remaining 1.5 lb. H<sub>2</sub>O per pound of sulfur burned must be provided in the subsequent chambers, occasionally as steam but more generally as water spray from atomizing nozzles, the object being to provide water of very small particle size.

**Gay-Lussac Towers.** These usually consist of two in series and are generally cylindrical, of about 8 lb. lead, lined with acid-proof masonry of about 12 in. wall thickness for the bottom third, 8 in. for the intermediate third, and 4 in. for the top third. Such towers were formerly packed with coke, but later stoneware in various

molded forms was substituted, thus permitting some reduction in tower area. Also, plate columns were used with considerable success for the first tower. The amount of tower space provided was about 2% of the cubic capacity of the chamber set.

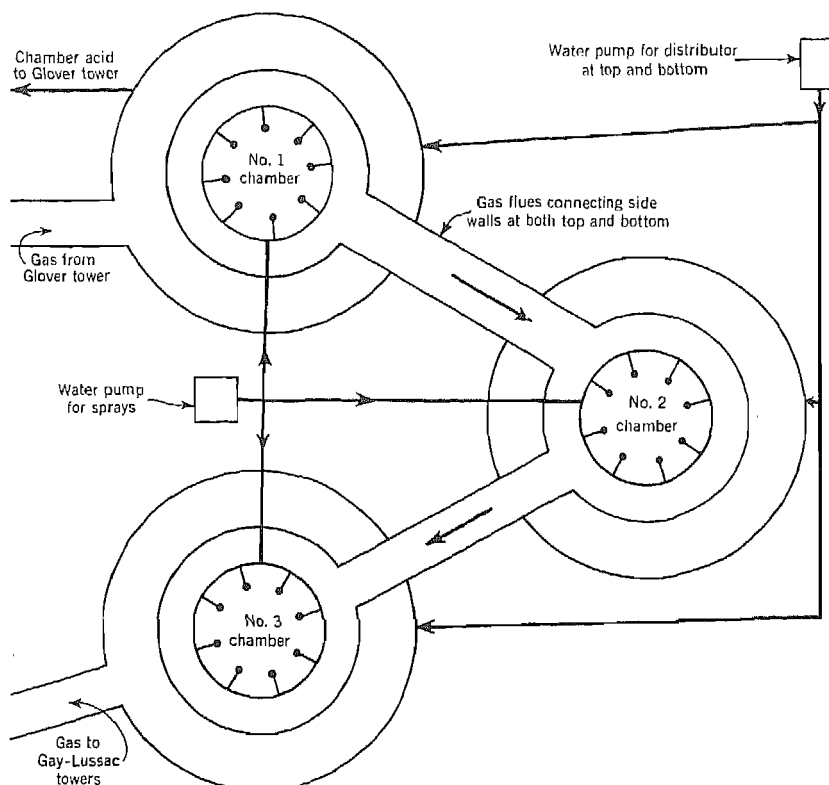
**Process Developments.** Critical study of the process disclosed that from 20 to 25% of the acid produced in the chamber operation was being formed in the Glover tower; indeed, the velocity of reaction in the denitration zone of the Glover tower was some 100 to 150 times that in the actual chamber space. The front part of the first chamber was also very active, but the reaction became sluggish in the back part. From 50 to 60% of the total acid was formed in the first chamber. Activity picked up a trifle in the front part of the second chamber, but then became sluggish again, and this performance was repeated on a constantly decreasing scale of activity through the remainder of the set. This reduced activity could be accounted for in part by the constantly decreasing sulfur dioxide content of the gas, but it was argued that the major reason was lack of adequate cooling and mixing of the gases. This led to numerous proposals looking toward a more intensive working of the chamber process which included installation of open, packed, or plate towers irrigated by weak acid, or towers containing cooling pipes, which were placed between chambers, and use of steam jets or fans to promote mixing of gases within the chambers. When the conventional lead chambers are eliminated, the process is often referred to as the *nitration process*.

*Meyer tangential chambers* were built in the form of cylinders, the gases being introduced tangentially and removed through a central flue. The rotary motion imparted to the gas promoted mixing and better utilization of the air-cooled chamber walls. This design never achieved popularity, for it was claimed that the life of the chambers was materially shortened by the action of the gases on the lead.

In contrast with the early rectangular chambers which were usually not over 25 ft. high and (except for moderate climates) completely enclosed by a frame building, *Falding* provided vertical chambers 50 ft. square by 70–80 ft. high, supported from a steel framework and erected in the open. Nitrous vitriol is sprayed into the chamber. A considerable number of such installations have been made both abroad and in the U.S. In many instances the plant consisted of one large chamber of this type followed by a second much smaller water-cooled chamber for cooling the gases, interposed between the Glover and Gay-Lussac towers. This design results in a considerable saving in ground space and lead, but with such a large unit the ratio of square feet of surface area to cubic feet of chamber space is about 1:10, and it has become generally recognized that heat radiating surface is as important a factor as cubic contents in determining plant capacity. These installations are reported to work satisfactorily with an allowance of about 7 cu.ft. chamber space per pound of sulfur burned per 24 hr.

A later development, and the most extensively employed both here and abroad, is the *Mills-Packard* water-cooled chambers, which are built in the shape of a truncated cone ranging in size from a base diameter of 20 by 40 ft. high to a base diameter of 35 by 50 ft. high, supported from a steel framework and also built in the open (Fig. 12). Radiating capacity of the lead walls is increased by flowing a film of water down the outside, and this also materially increases the life of the chambers. In some instances such chambers were installed in combination with the old rectangular chambers, but more generally the plant consists of such chambers exclusively, interposed between Glover and Gay-Lussac towers. With the smaller chambers, which provide a ratio of square feet of surface area to cubic feet of chamber space of about 1:4.0, a capacity as high as 2 cu.ft./lb. of sulfur burned per day has been realized, but

with the larger chambers where the ratio of surface to cubic contents has risen to about 1:7, the space requirement rises to from 4 to 5 cu.ft. chamber space per pound of sulfur burned per day. The capacity of the large chambers has been increased by providing an alley-way about 4 ft. wide down the center with vertical water-cooled side walls, thus converting the horizontal section from the original circle into two semicircles, thereby increasing the ratio of surface to cubic contents to about 1:4.3, virtually duplicating the advantages of the smaller chambers.



*Courtesy General Chemical Division, Allied Chemical & Dye Corporation.*

**Fig. 12. Mills-Packard water-cooled chambers** (three truncated cones, 25 ft. in diameter at the top; 30 ft. bottom diameter; 40–50 ft. in height).

*Gaillard-Parrish* chamber plants have been installed to a limited extent abroad. This system employs vertical chambers, from 40 to 60 ft. high, which may be either cylindrical or in the shape of an inverted truncated cone with a top diameter of 20 to 35 ft. and a bottom diameter only slightly smaller. In place of the indirect cooling of the Mills-Packard chamber, the Gaillard-Parrish system employs as its cardinal feature a Gaillard disperser, which is a high-speed centrifugal machine suspended from the center of the chamber top and by which a shower of externally cooled chamber acid is thrown against the chamber walls. More dispersers were installed in the old style rectangular chambers than in the specially designed Gaillard-Parrish chambers, and it was claimed the capacity of the old plants could thereby be increased about a third.

In addition to the modified chamber systems as described above, other systems

replaced the open chambers entirely by a series of packed towers over which externally cooled acid was circulated, thus making the cooling independent of surface area. A typical system was the *Opl system* used to some extent abroad but never in this country. Owing to the large contact surface provided by the wetted packing, the space requirement for this system is reported to be in the order of from 0.5 to 1.0 cu.ft./lb. of sulfur burned per 24 hr., but the amount of niter in circulation was greatly increased. Water required for the reaction was merely added to the recirculated acid. Usually such plants comprised six packed towers in series, the first three being considered as acid production towers, and the final three as niter-recovery or Gay-Lussac towers. A Glover tower preceded the first packed tower.

In the same class might be mentioned the *Petersen process*, also used fairly extensively abroad and usually comprising five masonry towers, the first designated as a denitration tower performing the function of the standard Glover tower, the second and third towers constituting the production towers, while the fourth and fifth function as Gay-Lussac towers for recovery of the nitrous oxides.

Also in this same general class might be mentioned the *Anaconda process*, which employed packed cells formed by partitions installed in a single masonry unit. This system, however, employed the conventional Glover and Gay-Lussac towers, the interposed "packed cell" tower being used as the production unit and being provided with a large circulation of externally cooled weak acid. Several plants of this type were built by Anaconda Copper Mining Company and its subsidiaries.

Under more intensive operation the circulating load of niter must be considerably increased, and this involves proportionally larger losses in niter recovery in the Gay-Lussac towers. Also, the tall chambers involve higher capital expenditure per cubic foot of chamber space than the original rectangular chambers, and where packed towers are employed, the resistance to the passage of the gas necessitates increased power consumption for moving the gas through the system, in addition to the added cost of recirculating the large tonnages of acid over the towers.

A detailed discussion of the chamber process will be found in Fairlie (1), including a complete description of modern practice. Although these modern systems constitute a substantial advance beyond the original horizontal chamber sets, the fact remains that the chamber or nitration process accounted for only 20% of the total production of sulfuric acid in the U.S. in 1952 as compared with 75% of the total production in 1921. Moreover, the contact process is gradually replacing the nitration process in the fertilizer industry, where acid above 60°Bé. strength is not required and where the nitration process is consequently in the best competitive position. Abroad the situation varies; in France, for example, as late as 1951 the nitration process still accounted for approximately 70% of the total sulfuric production.

The sulfuric acid produced directly in the lead chambers approximates 65%  $\text{H}_2\text{SO}_4$  (52°Bé.) which can be concentrated to about 78% (60°Bé.) in the Glover tower. The acid flows through the chamber set countercurrent to gas and is taken off the first chamber where it is lower in niter content and of highest concentration. The 60°Bé. Glover tower product is suitable for many industrial purposes, particularly for acidulation of phosphate rock, and as of 1954 about 25% of the total sulfuric production is used for manufacture of superphosphates which is identical with the percentage figure for 1935.

**Purification.** The quality of the acid produced in the process is, of course, dependent on the impurity content of the raw material employed. Acid produced

from brimstone contains chiefly a small amount of nitric acid, which for many uses is not objectionable. When the acid is produced from smelter gases or sulfide ores, however, impurities will vary considerably. Many sulfide ores are arsenical and, although this is not of great importance for fertilizer, acid containing arsenic is unsuitable for many industrial uses, particularly for manufacture of food products and for pickling of steel that is to be painted, tinned, galvanized, or enameled. This impurity may be removed by passing hydrogen chloride, which converts the arsenic to arsenic trichloride which can be volatilized below the boiling point of the acid, or by precipitation of the arsenic with hydrogen sulfide added as gas, or generated by addition of sodium sulfide. The hydrogen sulfide method also removes traces of nitric acid and also selenium, which imparts a red to pinkish color to the acid. Since

hydrogen sulfide is extremely toxic, it must be employed with the greatest care.

**Concentration.** Where acid stronger than 78% (Glover tower product) is required, it can be secured by concentration, but above 80%  $\text{H}_2\text{SO}_4$ , corresponding to 390°F. at atmospheric pressure, sulfuric acid is vaporized in ever-increasing amount until the constant boiling point is reached at 98.3%  $\text{H}_2\text{SO}_4$  when the composition of the vapor is identical with that of the liquid. A concentrator, therefore, must include means for recovery of the vaporized acid. Originally this concentration was carried out in platinum pans arranged in cascade form over a firebrick flue through which the hot gases passed to the stack. The pans were fitted with lead covers through which gases were carried to a condenser before evacuation to atmosphere. Later vitreous silica basins

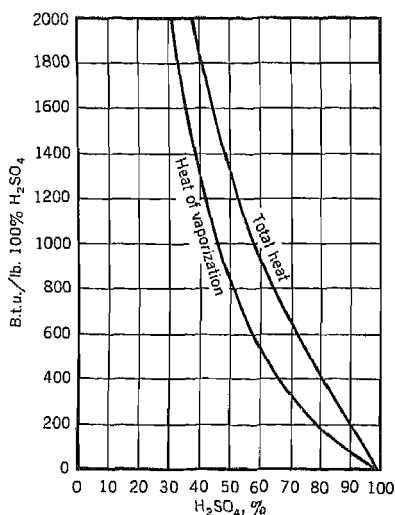


Fig. 13. Heat required to concentrate one pound 100%  $\text{H}_2\text{SO}_4$  from various strengths to 98.5%.

were employed, and occasionally cast iron pans when the concentration was to be carried above 92%  $\text{H}_2\text{SO}_4$  (10). Subsequently, the Gaillard tower was introduced (10). This is an unpacked tower into which acid is sprayed at the top, and passes counter-current to furnace gases. More recently, the concentration has been effected in apparatus such as the Simonson-Mantius vacuum evaporator, the Du Pont falling film concentrator, or the Chemical Construction drum concentrator. In the latest design of the latter, the high-temperature products of combustion are forced below the acid level in the drum which is a steel vessel lined with acid-proof brick. The stack gases are passed through an electrical precipitator before admission to the atmosphere. Thermal requirements for concentration as presented by Zeisberg (15) appear as Figure 13.

### Manufacture of Sulfuric Acid—Contact Process

Platinum was the catalyst originally discovered by Phillips in 1831 and was employed in all the early commercial applications around 1900. Although use of other materials, such as the salts of vanadium and silver, ferric oxide, chromium oxide, and

some of the rare earths had been proposed, none of these substitutes possessed the activity of platinum or were capable of carrying the reaction so nearly to completion, and consequently platinum alone was found capable of providing satisfactory yields.

Values of the equilibrium constant for the reaction  $2\text{SO}_2 + \text{O}_2 \rightarrow 2\text{SO}_3$  are shown in Figure 14. Substantially 100% conversion is obtainable at 715–750 F., provided the catalyst is sufficiently active and the time of contact is sufficient. Figure 15 reproduces curves presented by Knietzsch (5) that show the effect of time of contact with a platinum catalyst. Taking both equilibrium and time of contact into consideration, it will be evident that although optimum conversion will be obtained at 715 to

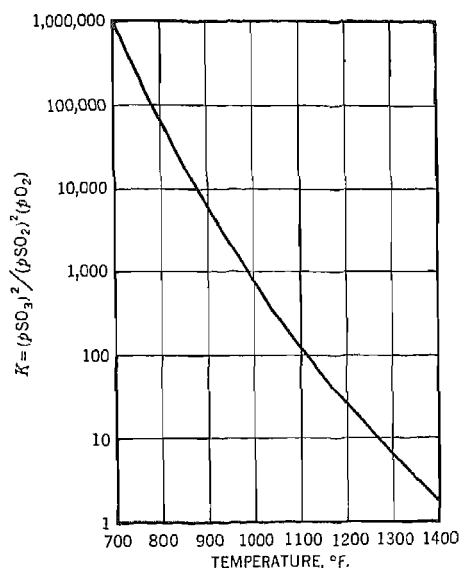


Fig. 14. Equilibrium constant for  $2\text{SO}_2 + \text{O}_2 \rightarrow 2\text{SO}_3$ .

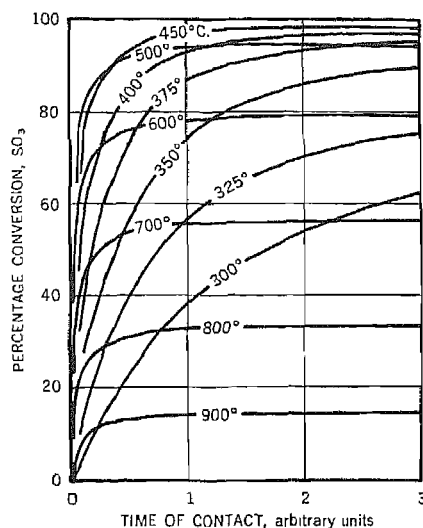


Fig. 15. Relation between conversion and time of reaction at various temperatures.

750°F., maintenance of that temperature throughout the reaction would require excessively long contact. From a practical point of view, a great saving in contact mass can be secured by doing the major part of the work at a higher temperature, where a much higher reaction velocity is obtained, and then completing the reaction in the lower temperature range to secure optimum overall conversion.

In contrast to the chamber process, the contact process from the start was based on the use of sulfide ores, rather than brimstone, and the tremendous effort that was expended in the development of the process between 1875 and 1900 was due to the fact that the catalyst was subject to rapid impairment. Painstaking research on the causes of catalyst deterioration and development of methods to prevent it finally resulted in an elaborate procedure for purification of gas prior to conversion. Platinum is extremely sensitive to poisoning, and the amount of arsenic, for example, in the gases supplied to the platinized asbestos catalyst should not exceed about  $0.3 \times 10^{-6}$  g. As per cu.ft. to avoid gradual loss of catalytic activity.

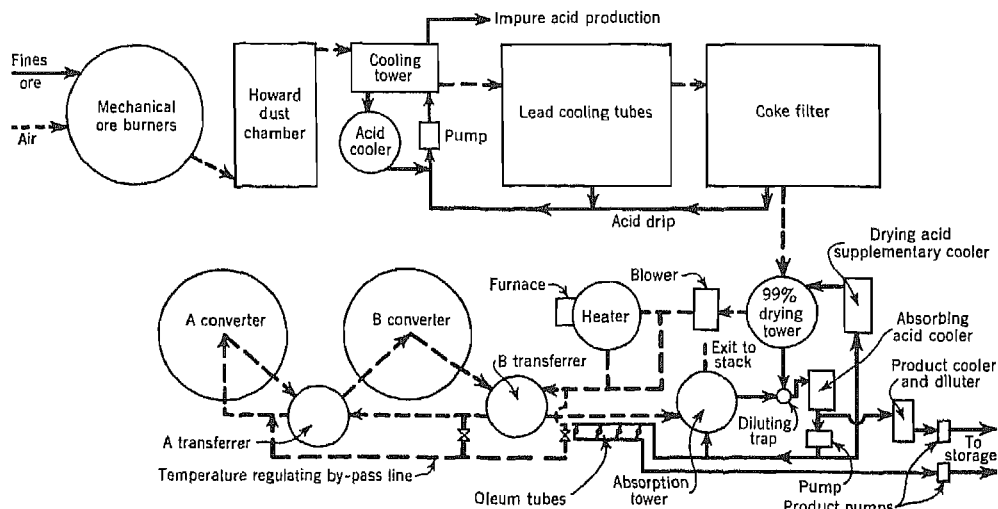
Production methods have followed the general trend of American industry to units of larger size. Starting with the earliest contact units of 20 tons sulfuric daily

capacity, a modern unit may provide upwards of 250 tons daily capacity. The term unit refers primarily to the converter assembly, as the complete plant will usually include several drying and absorbing towers in parallel, and in an ore-burning wet purification plant may include several scrubbers and coke filters in parallel.

In addition to effecting a material saving in fixed capital requirements, the large unit also effects a corresponding reduction in process control, and this has been even further reduced by instrumentation. The instrument panel, in a central control room, shows plus, minus, and differential pressures at various points through the system, boiler pressure and boiler water level indicator, sulfur dioxide concentration, etc., and high and low level alarms are provided for the various pump tanks, or to call attention to any irregularity in distribution of acid over towers. One multipoint recorder will provide interrupted lines for a continuous record of all pertinent temperatures throughout one conversion unit, and another recorder can be used to provide a record of other gas and acid temperatures through the system. Strength of acid in circulation over the various towers is shown by a pointer on large clocklike dials, and an attached pen makes a continuous record on the chart. The same instrument can be arranged to regulate diluent automatically to maintain strength at the desired point.

#### WET GAS PURIFICATION

The objective in gas purification is to provide a mixture of sulfur dioxide, oxygen, and nitrogen virtually free of all solid, liquid, and gaseous impurities. This is effected



*Courtesy General Chemical Division, Allied Chemical & Dye Corporation.*

**Fig. 16. American type Badische contact unit.**

in a series of steps comprising: (a) dust removal; (b) cooling and scrubbing; (c) mist removal; and (d) drying. See Figure 16.

**Dust Removal.** Solids must be removed from the gas as a first step, since the packed towers, filters, etc., employed in subsequent steps would otherwise rapidly become plugged. The magnitude of this problem is primarily determined by the physical character of the raw material and particularly by the type of apparatus employed in roasting the ore. The lump ore burners employed in the earliest plant installations



produced very little dust, and even with the mechanical burners, such as the Herreshoff and Wedge, operating on fines passing through a  $\frac{3}{8}$ -in. screen, the dust leaving the burner rarely amounted to more than about 4.5% of the total cinder, but this was more than could be tolerated in scrubbing towers and resulted in the application of the hot Cottrell and the Howard dust chamber, with the dusty gas in the range of 850° to 930°F. to avoid condensation and sulfation. The early Cottrell installations were not too favorably received in this country, but the Howard dust chamber was very extensively employed. The first design, employing horizontal plates, was later superseded by installations with inclined plates to facilitate cleaning, but the improvement was nominal. These chambers were built in units comprising six to seven compartments, separated by brick walls which permitted cleaning of one compartment while the others remained in use. Average schedule called for each compartment to be cleaned once a week while handling the dust from 10 net tons of fines per day.

When the very finely divided flotation concentrates became available, they were at first roasted in mechanical burners and, although the dust content of gas increased appreciably, the Howard dust chambers were able to handle the load; but with the advent of the flash or suspension roaster the percentage of the cinder leaving the roaster in the gas stream rose to 50% or more. While one-fourth to one-third of this mechanically carried dust would drop out in the waste heat boiler following the burner, a tangential dust collector (cyclone) is usually installed next in line, although electric precipitators are frequently employed. The efficiency of an electrical precipitator is not affected by particle size, but the centrifugal separator employs radial acceleration to effect separation of suspended particles. Since particle size controls the optimum diameter of the individual cyclone unit, it is advisable, when dealing with very fine dust, to employ a unit comprising a number of small tubes in parallel. This will give satisfactory efficiency at reasonable tangential velocity, which is the determining factor in power requirement. See also *Gas cleaning*; *Electrostatic precipitation*.

**Cooling and Scrubbing.** Gas leaving the suspension roaster at about 1800°F. is rapidly reduced to about 700°F. in the waste heat boiler, permitting employment of ordinary steel collectors. Assuming reasonable separation efficiency, the gas can then be admitted to a brick-lined scrubbing tower where, as a result of evaporation of water from the scrubbing acid, the gas temperature is further reduced to about 250°F., and the major part of the remaining dust is removed. The scrubbing acid is cooled prior to recirculation, and is recovered as an off-grade product, which has a limited outlet for certain industrial uses, as in fertilizers. Cooling of the gas is then continued to approximately atmospheric temperature in vertical unlined lead tubes, cooled by a film of water on the outside. The tubes are arranged both in parallel and series, the distribution being determined by the volume and water content of the gas. When ores either of high arsenic content or containing fluorides are roasted, the major portion of the arsenic or fluoride is deposited in these tubes. The headers are fitted with removable covers at the ends so that the cooler can be flushed out periodically. The number of tubes in parallel in successive passes should be gradually reduced in direct ratio to the contraction of the gas through cooling and condensation. A properly designed installation of 8 in.-diameter vertical tubes will provide a heat transfer coefficient of 8 B.t.u./(hr.)(sq.ft.)(°F.). The quantity of water that can be supplied to such a cooler is naturally limited by the thickness of film that will remain in contact with the lead tube.

As an alternative to such indirect cooling, the gas may be cooled by direct con-

tact with water, achieved through use of water sprays and packed towers; but in order to avoid creation of an atmospheric or stream pollution problem the cooling water, which will contain an appreciable amount of dissolved sulfur dioxide as well as condensed acid, must be either indirectly cooled, stripped of its sulfur dioxide content in separate apparatus, and recirculated, or else neutralized with consequent loss of yield.

A decided advantage of indirect cooling arises from the fact that the condensate from successive passes varies considerably in acidity, and when operating on a tight water balance, segregation of drips permits discard of the maximum amount of water with the minimum loss of acid. Similarly, when gases contain impurities such as fluorine, as much as 95% of the fluorine content can be eliminated with loss of no more than about 15% of the sulfuric acid content of the total cooler drip.

**Mist Removal.** The gas at this point can be assumed to be free of impurities other than water vapor, sulfuric acid, and those carried in the sulfuric acid mist. This mist is a carrier for arsenic, and would in any case cause corrosion. It can be removed either by filtration or electrical precipitation. While many materials such as quartz, sand, rock wool, coal, pumice, asbestos, saw dust, wood shavings, and coke have been employed from time to time, none have equalled the efficiency of coke. This should be 72-hr. hard-burned beehive oven coke, free of soft and tarry knots, broken down and screened to five size ranges.

The filter is usually constructed as a rectangular lead-lined wooden box of approximately 1000 sq.ft. area, fitted with a grid tile carried on brick or tile supports about a foot above the bottom of the box. The largest size coke is spread over the tile and carefully levelled off before placing the next size in position, continuing in this manner with the smaller sizes until the packing reaches a total depth of about 8 ft. It is important both from the standpoint of efficiency and resistance that mixing of sizes be avoided.

Should the gas entering the filter contain any solids, or should the ores contain lead, it is advisable, if not necessary, to protect the main filter by a preliminary or scalper filter, which may be packed with an intermediate size coke carried on slotted lead sheets. Even if the gases contain no impurities other than sulfuric acid and water, the preliminary filter is still advisable as it will relieve the main filter of much of the condensation of weak acid, thus freeing it for the more important work of mist removal. The main filter can be satisfactorily operated at rates between 3 and 6 c.f.m./sq.ft. box area, and the primary or scalper can be operated at somewhat higher rates. Pine excelsior placed on a wooden grid has also been used successfully in the primary filter though it does not equal the efficiency of coke.

In some contact installations a number of small filters, ranging between 50 and 100 sq.ft., have been provided, with the idea that small units could be cleaned and repacked with less interruption to production. However, the overall cost of such an installation is much higher; it involves more time of the operator in checking resistances and flow rates, and is unnecessary since, if the gas entering the main filter is free of solids as it should be, such filters can be operated for 20 years or longer without washing or repacking. The preliminary or scalper filter, however, will require cleaning or repacking, where a material like excelsior is employed, as frequently as monthly to semiannually, depending on the impurity content of the entering gas.

Gas leaving the main filter should contain not more than 0.000075 g.  $\text{H}_2\text{SO}_4$  and

1.00 g.  $\text{H}_2\text{O}$ /cu.ft. No cooling of the gas should take place between the filter and the drying tower as the condensation that occurs will result in oxidation of sulfur dioxide with formation of additional mist.

Electrostatic precipitation is employed extensively for removal of sulfuric acid, and in addition to the standard Cottrell precipitator, other types, such as that employing the Kenetron tube rectifier, have been proposed more recently. A correctly designed Cottrell will provide satisfactory performance, but fixed capital requirements offer little, if any, saving over the coke filter and it is more subject to interruptions in service. Both Cottrell and coke box have their advocates, but it would seem that the filter offers greater opportunity for progress through the medium of improved design and filter material.

**Drying.** As a final step in the wet purification train, the moisture content of the gas should be reduced to a figure between 0.005 g. and 0.010 g.  $\text{H}_2\text{O}$ /cu.ft. and certainly not higher than 0.015 g.  $\text{H}_2\text{O}$ , as anything above that value will not only increase corrosion of subsequent apparatus, but in addition will most likely cause formation of sulfuric acid mist that will result in a visible absorber exit.

This drying is accomplished in packed towers irrigated by drying acid which may be either 99%, 66°Bé. (93%) or 80–85%. Use of 99% acid has the advantage of combining the drying system with the absorbing system, thus eliminating a separate acid circulating system. A portion of the absorbing acid is subjected to supplemental cooling in a cast iron cooler and is then sent to the drying tower. Acid leaving the drying tower is combined with that from the absorber. The drying tower is of steel, lined with acid brick, and set in acid-proof cement.

Another extensively employed system utilizes 66°Bé. acid for drying. This avoids the use of lead or lead-lined equipment, the drying tower being of steel lined with acid brick, and the acid cooling and circulating system of cast iron. Corrosion of the cast iron equipment, however, is more severe than when employed for 99% acid, and this system does not lend itself readily to production of low-iron acid.

A very extensively employed drying system uses acid ranging from 80 to 85%, depending on temperature. This method requires an independent acid circulating system comprising a steel tower, lead-lined and preferably also brick-lined, in conjunction with all lead acid circulating lines, pump, tank, and coolers which latter should be adequate to deliver acid to the tower cooled to no higher than 100°F. Acid is maintained at desired strength by continuous interchange with absorbing acid.

Gas dried in this manner is free of the fume that is associated with 99% drying and that results in increased maintenance by the corrosion of blowers and flues and plugging of converters with the deposited sulfate. Although the weaker acid does not have the avidity for water of 99% acid, there is no difficulty in reaching equilibrium in a properly packed tower, taking care that the proper strength of acid is used, according to the temperature and the amount of water to be left in the gas. Before leaving the tower the gas can be passed through a basket containing steel wool or glass wool to remove any mechanically carried spray.

**Blowers.** In the wet purification process, the blower is placed between the drying tower and the conversion unit, since it is then handling a purified and dried gas at approximately atmospheric pressure. Positive displacement blowers of the Roots type are preferred, although centrifugal blowers have been employed in many installations.

## HOT GAS PURIFICATION

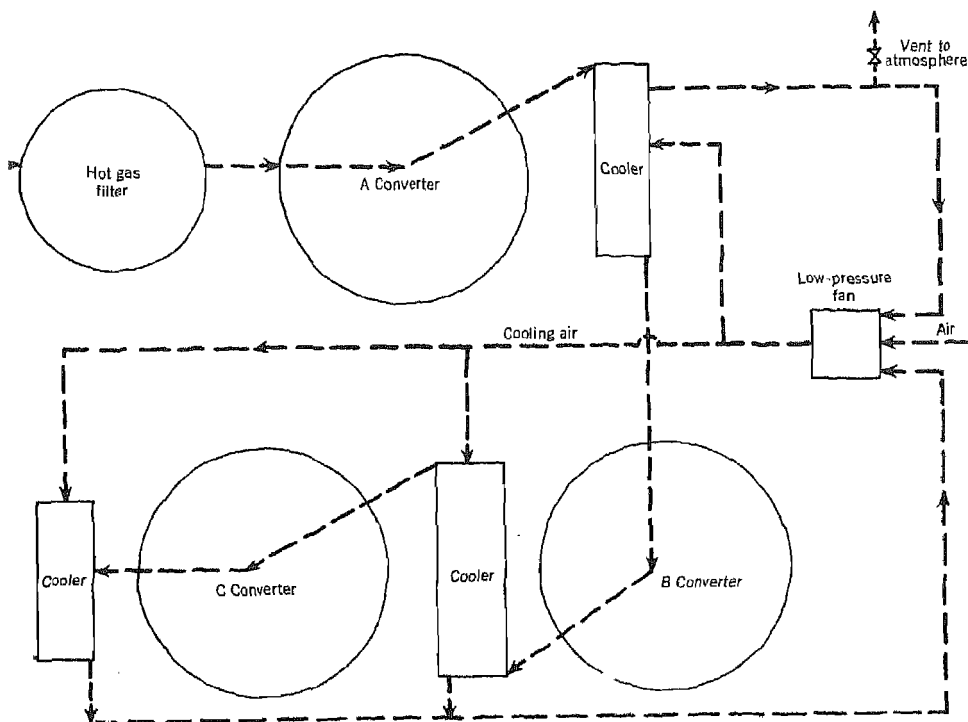
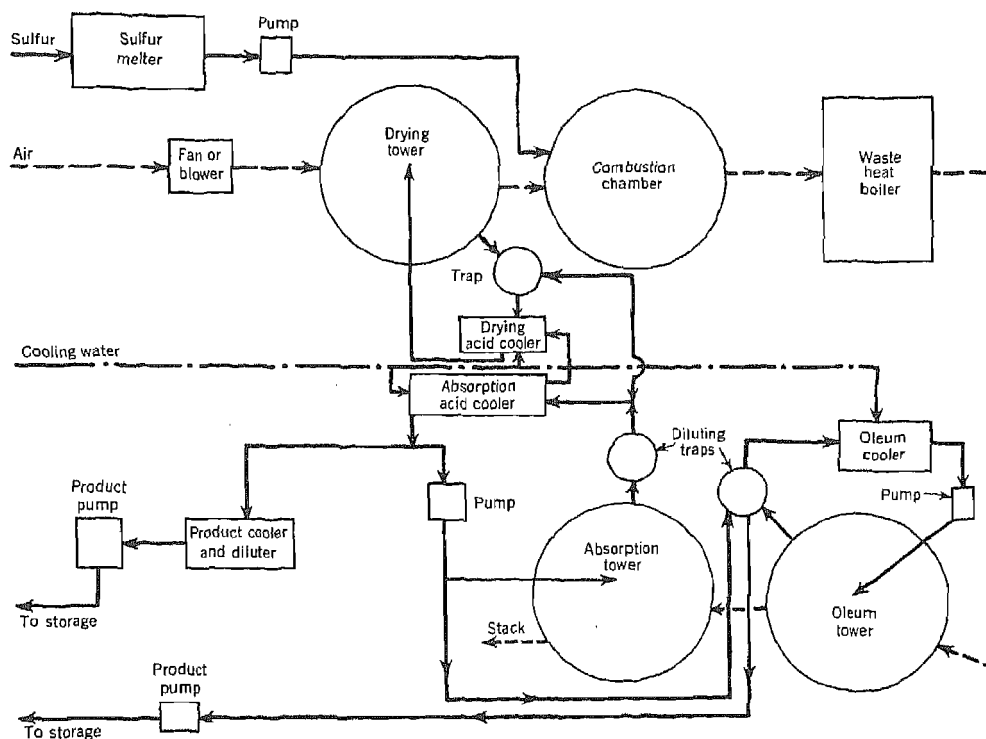
After World War I a change-over was made from pyrite to Louisiana brimstone. In many ore-burning plants, brimstone was burned in the lump ore burners and mechanical roasters, and the gas was subjected to the customary wet purification procedures, but it was found that this gas contained such a low content of impurities that exerted a poisoning effect on platinized asbestos that the wet purification procedure could be dispensed with. The gas was treated by hot gas purification (Merriam process) (16), in which at no point in the process subsequent to combustion of the brimstone is the gas permitted to drop below the temperature at which condensation could occur. Purification is actually limited to the use of a filter placed before the first converter to remove solids suspended in the gas stream. The first large unit of this type, with an annual capacity of 50,000 tons, was erected in the winter of 1925-26. The blower or fan was placed at the front end of the system handling air which was passed first through a drying tower to dry it to about 0.005 g.  $\text{H}_2\text{O}/\text{cu. ft.}$ . If the air were not dried, then if at any later point in the process the gas should fall below the condensation temperature, there would be danger of severe corrosion in the coolers (see below under "Conversion") and of the formation of a mist in the absorbing system which would pass out the exit stack. After the dryer, the following apparatus is arranged in series: sublimers and combustion chamber, cast-iron pipe radiator, and filter, after which the gas was handled in the standard conversion and absorption system. After a brief trial of a dry sulfur feed to the sublimers, the brimstone was melted and impurities settled out, and the sublimers were supplied with the molten purified sulfur. More recently the molten sulfur has been filtered, although from an overall cost standpoint it is questionable whether this offers any appreciable advantage.

The hot gas purification system reduced the cooling requirement of the drying system to from 20 to 60% of that of the wet gas system, depending on the geographic location of the plant, and reduced the fixed capital expenditure for a contact acid plant to about 40% of that required for an ore burning plant with complete wet purification system. Shortly after operation of the initial unit, a waste heat boiler was incorporated in the design, providing a substantial power credit. See Figure 17.

## CONVERSION

**Platinum Catalysts.** The contact process was born and reared on platinum catalyst, since it was the only material capable of providing a commercially acceptable rate of conversion. The Mannheim process employed a first stage utilizing ferric oxide, but conversion rarely exceeded 40% and it was necessary to employ platinum in subsequent stages. Of the many materials employed as supports or carriers for platinum, only magnesium sulfate (Grillo mass), silica gel, and asbestos have stood the test of time, the latter being by far the most frequently employed, and incidentally the original Badische catalyst.

Long-fiber asbestos (chrysotile), after a preliminary washing, is dried and carded and then immersed in a solution of chloroplatinic acid (hexachloroplatinic(IV) acid),  $\text{H}_2\text{PtCl}_6$ . After draining and drying, it is repeatedly fluffed in a carding machine until matted material is pulled apart, and finally fluffed by hand by means of tweezers. The finished material may contain from 5 to 10% Pt by weight, and is customarily employed in an amount approximating 0.015 troy oz. (0.461 g.) of Pt per ton of annual capacity. When the catalyst mass is first put on stream, the chloroplatinic acid is decomposed to platinum black.



Courtesy General Chemical Division, Allied Chemical & Dye Corporation

Fig. 17. Hot purification contact unit.

Magnesium sulfate is subjected to a double calcination to produce a hard mass which is crushed and screened to approximately  $\frac{3}{8}$  to  $\frac{1}{2}$  in. in size. The cold mass is then sprayed with a solution of chloroplatinic acid in such amount that the platinized mass will contain about 0.25% Pt by weight, with the same Pt requirement per ton of acid as platinized asbestos.

Silica gel, prepared as a hard granular material, is sprayed with a compound such as ammonium chloroplatinate in an amount sufficient to provide from 0.075 to 0.125% Pt by weight, and the platinized gel, after drying, is ready for use in the converters. Platinum provided per ton of acid produced is lower than in the case of the other platinum catalysts but, as the silica gel is quite expensive, the overall cost of the prepared catalyst is substantially higher.

Contaminated Grillo mass can be reactivated several times by spraying with aqua regia and recalcining, but platinized asbestos is too fragile to stand removal from the converter. If blanketed by a deposit of iron sulfate, the resistance can be largely removed by reverse blowing with a current of air, but if poisoned by arsenic, there is no known procedure by which activity can be restored. Silica gel is claimed to be immune to arsenic poisoning and is only temporarily poisoned by chlorine, but it is disintegrated by fluorine compounds. This particular catalyst appears to have found wider use abroad than in the U.S.

Up to about 90% of the original platinum can be recovered from any of the above catalysts whenever loss of activity necessitates replacement.

**Vanadium Catalysts** (Ref. 1, p. 413). The use of vanadium as a catalyst for the oxidation of  $\text{SO}_2$  to  $\text{SO}_3$  was first discovered by DeHaen, who took out a patent in Germany in 1900, but the activity of his catalyst was too low to be of commercial importance. It remained for Slama and Wolf (18) to develop a commercially successful vanadium mass which was employed in large commercial units by Badische Anilin und Soda Fabrik beginning in 1915, and by 1928 had completely replaced platinum in all converters of this company. It was not until 1927 that vanadium catalyst was employed commercially in the United States. The Slama-Wolf patent disclosed and claimed a catalyst consisting of a carrier, such as powdered pumice or kieselguhr, with particle size less than 60 microns, with which the catalytic agent of vanadium pentoxide and potash was combined. The mass was prepared with a consistency which permitted compression into tablet or pellet form and later was formed into worms by extrusion.

Although the particle size of the carrier has been emphasized, it appears that the combination with vanadium of an alkali, which has been variously referred to as a stabilizer or promoter, is of great importance. Under converter operating conditions the alkali with which the vanadium is combined appears to be in the form of bisulfate and when this is so, the vanadium is capable of migration. This can readily be demonstrated by preparing worms or pellets identical in every respect, except that half the mass would contain no vanadium. After a relatively short period of operation, it will be found that all pellets have about the same vanadium content.

Vanadium catalysts are complex compositions containing vanadium in the oxidation state corresponding to  $\text{V}_2\text{O}_5$ . Before being put on stream, they must be heated in a low concentration of sulfur dioxide, since the conversion of the alkalies present to sulfates or bisulfates is strongly exothermic.

Between 1925 and 1927, vanadium contact masses were developed for Monsanto Chemical Company and the Selden Company by former employees of Badische

Anilin, and, as the U.S. counterpart of the German Slama-Wolf patent was assigned to General Chemical, all three of these companies became involved in extensive patent litigation.

**Vanadium versus Platinum.** Many conflicting statements have been published with respect to the relative merits of platinum and vanadium catalysts in the contact process. Aside from the admitted sensitivity of platinum to poisoning, it has been stated by some that the conversion efficiency of vanadium catalyst exceeded that of platinum and was cheaper, while others contended that vanadium required a larger excess of oxygen than platinum and gave lower conversion on gases of equal concentration.

Platinum possesses much greater catalytic activity than vanadium and is active over a much wider temperature range. The ignition temperature (lowest temperature at which a vigorous reaction will take place) of an average vanadium mass may approximate 800 to 805°F., whereas a good platinized asbestos catalyst will have an ignition temperature at least 70 to 90°F. lower, and this affects the conversion in two ways, as follows:

In a large well-insulated unit, each 1% by volume of SO<sub>2</sub> converted will produce a temperature rise of about 50°F., from which it follows that from 1.5 to 2% by volume of SO<sub>2</sub> can be converted in the first platinum converter by the time the temperature has reached the point at which the gas would have been admitted to the vanadium converter. The reaction will be halted at the equilibrium curve, and a vanadium catalyst, on a 10% SO<sub>2</sub> gas from brimstone, will give 60% conversion in the first converter, but a platinum catalyst, with the extra 2% of SO<sub>2</sub> converted, will give 80% conversion. Thus the vanadium catalyst will necessitate the use of an additional stage.

The top range of the conversion is affected in the same way. An overall conversion of 98.25% can readily be secured in the final platinum converter on an 11% SO<sub>2</sub> gas from brimstone, which would contain only 4.5% free oxygen after conversion. The reaction, however, would have to be completed within the range of 780 to 790°F., at which platinum possesses good activity. Under these conditions, vanadium catalyst would be so sluggish as to make the operation impracticable. On raising the temperature to about 830°F., at which vanadium would have satisfactory activity, the maximum conversion obtainable would drop to 97.25%.

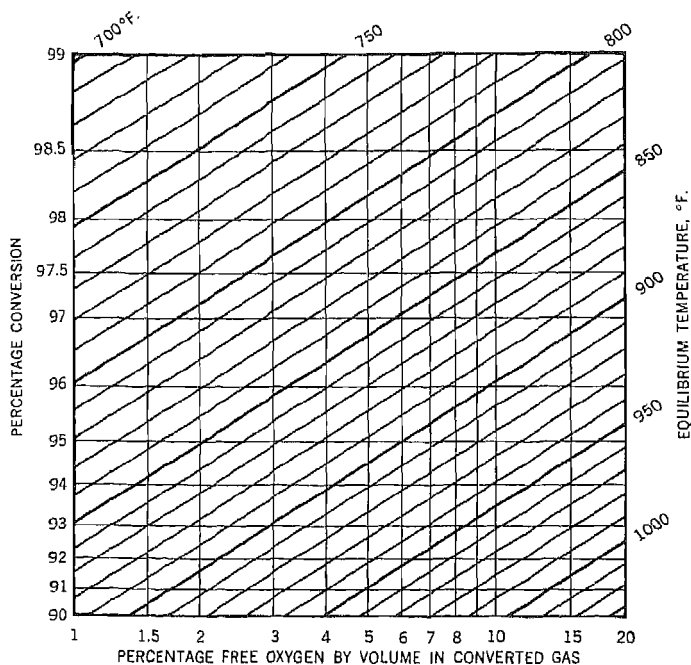
On the other hand, if the 11% gas is diluted with air to a 7% SO<sub>2</sub> basis, which would provide 10.6% free O<sub>2</sub> after conversion, then the vanadium mass at the same 830°F. temperature will provide the desired 98.25% conversion.

Conversion equilibrium is determined by the temperature and free oxygen content of the converted gas and is independent of the catalyst. The influence of these factors is shown in Figure 18 which covers the range of 90 to 99% conversion. It will be obvious that to secure the desired conversion at higher gas concentrations implies use of a catalyst that is active at the necessary reaction temperature. The alternative is to raise the oxygen content the necessary amount to permit use of the desired catalyst at a temperature at which it is active.

The susceptibility of platinum to poisoning is overemphasized, since, even if the sulfur dioxide originates with a sulfur-bearing ore rather than brimstone, the gas will in any case have to be purified and the mist removed to protect subsequent apparatus. One disadvantage of vanadium is that it cannot be economically recovered from discarded mass. However, the preparation of a good vanadium mass is relatively simple as compared with platinized asbestos. Perhaps the matter can best be summed up

by observing that the large acid producer who has the "know-how" to produce and use either catalyst will select vanadium, since, owing to its much lower cost, it can be used more freely.

**Converters.** The early Badische converter consisted of a brick or steel vessel containing a bundle of parallel steel tubes; the platinized asbestos being supported on perforated plates placed within the tubes and separated by spacers, and the Tentelew converter followed the same general design. As modified by American practice, the



*Courtesy General Chemical Division, Allied Chemical & Dye Corporation.*

**Fig. 18.** Conversion as a function of equilibrium temperature and free oxygen.

converter was a cast iron or steel vessel about 7 ft. in diameter, and the catalyst was carried on perforated steel plates separated by 1 in. pipe spacers.

Operating on a pyrite gas of about 8.5%  $\text{SO}_2$  content, some units are provided with three converters in series and other units with only two, which latter, with active catalyst, give approximately 96% overall conversion. With a total provision of 70 to 80 plates, of which about 25 are in the first converter, about 80% conversion is obtainable from about 10 plates, where reaction is stopped by the temperature rise. (The remaining 15 plates in the first converter are a factor of safety so that, with gradual deterioration of the catalyst, the converter will have a long life.) It is then necessary to cool the gas to about 750 to 780°F. before entering the second converter. This cooling is effected by heat exchange with incoming cold gas, utilizing boiler-like tubular vessels called "transferrers"—one placed between each converter and one following the final converter.

Used in conjunction with a wet purification system, the gas from the blower at about 95 to 100°F. is passed through the transferrers in series before entering the first converter. Temperature regulation is secured by valves located in by-pass lines in-



stalled across the transferrers. The transferrers are fitted with baffles, and it is customary to pass the converted gas through the tubes since they can be readily cleaned.

When a brimstone gas is employed in a hot purification unit, the gas is *cooled* (against air) before entering the first converter, and again between converters. More converters are required in series to obtain the desired overall conversion if it is desired to take advantage of the higher sulfur dioxide concentration possible when burning brimstone.

For use with platinized magnesium sulfate, a cast-iron cylindrical converter either consisting of flanged and bolted sections or containing superimposed shelves or trays is employed. Two converters, each containing 5 to 6 trays on which the catalyst is spread to a depth of 9 to 12 in. are employed in series. These vessels may be jacketed to permit heating up when the unit is started and cooling during operation.

Vanadium mass is employed in solid beds that may vary from 20 to about 50 in. in depth, supported on a screen placed over a cast-iron or steel grille. The vessels may be cast iron but are usually steel, the size being determined by the capacity of the unit. It is customary to provide 1 sq.ft. converter area per 75–100 c.f.m. (N.T.P.) gas volume. Many converters containing platinized asbestos have been utilized for vanadium mass by replacement of the perforated plates with a screen covered grille on which the mass is dumped.

Converter systems are of two general types: one employing internal heat exchange by means of cooling tubes embedded in the catalyst, the other utilizing external coolers installed between converters.

Since the reaction velocity increases with temperature, maximum utilization of catalyst would be achieved by raising the gas temperature initially to about 1000°F., and then continuously removing heat produced by the reaction plus additional cooling so as to maintain the temperature at that required for a favorable equilibrium. In practice, however, this theoretical advantage cannot be realized since it requires continuous maintenance of preestablished conditions of gas concentration, volume loading, oxygen ratio, and catalyst activity. Greater flexibility is secured through external cooling, so that changes in these factors can be compensated for by adjustment of valves in by-pass lines across the coolers. In such a system, however, if overall conversion of the order of 98% is desired, the sulfur dioxide content of the gas entering the final converter should not be appreciably in excess of 0.80%.

Converters and transferrers are always well insulated, not only to conserve heat, which is quite important in the wet purification unit, but also to prevent the condensation and corrosion that would result on contact of the converted gas with a cool metal surface.

Preheaters were employed continuously in the early contact units to bring the gas up to the catalyst ignition temperature. In the modern large unit with well-insulated vessels, the operation is self-sustaining with a gas concentration as low as 6% SO<sub>2</sub>, and the heater is normally employed only for restarting the unit after a shutdown. The heater is a steel tubular vessel in a fuel-fired furnace.

#### ABSORPTION

**Absorbing Towers.** The converted gas is absorbed in strong sulfuric acid which, for best results with respect to absorption and low iron content, should approximate 99.0 to 99.2% H<sub>2</sub>SO<sub>4</sub> in its final contact with the gas. Absorption is usually carried out in a packed tower, and the absorbing acid is recirculated by means of a cast iron

pump at a rate that will permit a strength rise in the tower of not over 0.6%  $\text{H}_2\text{SO}_4$ . The acid leaving the tower is diluted back to its original concentration with water or weak acid. The electrical conductivity of the acid (Fig. 4) is utilized to determine and continuously record the strength of the acid in circulation, and, if desired, maintain strength automatically by mechanical regulation of diluent.

In the conventional wet purification unit, the converted gas leaving the final transferer will not exceed about  $680^\circ\text{F}$ . and can be admitted directly into the absorber. In the hot purification unit, gas leaving the final converter at perhaps  $825^\circ\text{F}$ . should be partially cooled prior to absorption; otherwise a visible exit gas will result. This cooling should be effected in an air-cooled tubular vessel, and not by radiator pipes installed in the open where they would be wetted by rain. Overcooling of the gas will result in formation of sulfuric mist that will create a visible exit gas.

Towers in which the absorption is carried out are frequently steel, lined with acid brick set in an acid-proof cement. Since it is very difficult to provide a lining that will remain tight over a long period of service, many towers consist of flanged cast-iron sections bolted together. Such towers are unlined and are virtually unattacked by acid of proper strength and temperature. The towers are packed with quartz pebbles or one or more of the many forms of ceramic packing that are available.

In some instances, several towers are employed in series, but this is unnecessary if packing, gas loading, and acid circulation and distribution are such as to permit reaching equilibrium between exit gas and inlet acid. Uniform distribution of acid over the tower area is most important, and is most easily secured by providing numerous points of distribution such as distributor tubes or pipes at uniform spacing. An effective method is to set the tubes in acid-proof cement in a cast-iron distributor plate on which acid is maintained at a depth of 6 to 10 in. The tubes should be high-silicon iron.

Absorbing towers are sometimes followed by a packed tower operated dry for removal of entrained acid, which, however, does not eliminate the sulfuric mist that is responsible for a visible exit gas. Many units are equipped with a Cottrell precipitator for removal of this mist.

**Acid Coolers.** The heat produced in the absorber is continuously removed by a cast-iron cooler incorporated in the acid circulating system, occasionally on the outlet side of the pump, but usually for safety reasons installed between the tower outlet and the pump. To obtain a good heat transfer coefficient, the cooler design should provide for frequent and abrupt changes in direction of flow of the acid. Better results will be secured by covering the cooler surface with a film of water supplied from a distributor box, or by spray nozzles, rather than immersing the cooler in a tank of water.

The demand for 99% acid is limited by its high freezing point,  $40^\circ\text{F}$ . The major demand is for 66°Bé. acid (93.19%). The absorbing acid is, therefore, diluted with water or weak acid and the heat of dilution removed in a product cooler. A cooler of the type employed on the absorbing acid is generally used, with due allowance for fact that the output of the unit is ordinarily not more than 1.5% of the circulating load on the absorber.

#### OLEUM PRODUCTION

Oleum is obtained by maintaining the absorbing acid in contact with the sulfur trioxide-containing converted gas until the desired concentration is built up. In

modern practice the acid is recirculated over packed towers of relatively large diameter, and the heat of absorption is removed in external coolers, as in the production of 99% acid. The towers are of steel, usually lined with acid brick, although unlined towers will give many years of service. Oleum systems may include from one to three towers placed ahead of, and in series with, the final absorber, depending on the strength of oleum desired, and the sulfur trioxide content of the gas available.

As in the case of 99% acid, the electrical conductivity of the oleum (Fig. 8) is utilized to determine, record, and if desired, automatically regulate the diluent to maintain the desired strength of product.

As will be noted from Figures 5 and 6, the vapor pressure of oleum rises rapidly with strength and temperature. During the second World War, 40% oleum was employed exclusively in production of T.N.T. and D.N.T., and virtually every contact plant in the eastern half of the U.S. was utilized in producing 40% oleum for the manufacture of high explosives. Approximately 97% of this tonnage was recovered as a weak, impure acid that after denitration was concentrated to about 66°Bé. About 40% of this concentrated recovered acid could be fortified with dry sulfur trioxide to reproduce the original tonnage of 40% oleum. The remainder of the recovered acid was either used for industrial applications in which its color was not objectionable, or else shipped to sulfuric acid manufacturers, where it was decomposed in a furnace and the sulfur dioxide used to manufacture sulfuric acid.

Since in the production of 40% oleum the recirculated acid has a freezing point of 99°F., it is not practical to cool it below 105°F. and in practice, the gas leaving the 40% tower will contain about 5.25% SO<sub>3</sub> by volume, and only the sulfur trioxide in excess of this figure can be absorbed. It is, therefore, the practice to follow the 40% tower with an intermediate tower having an independent acid circulating system, the product from this tower providing the diluent for the 40% system. The strength maintained on this intermediate system will approximate 25% oleum, and the residual gas sent to the final 99% absorber may vary from about 2.5 to 3.5% SO<sub>3</sub>.

When 40% oleum must be produced in a plant in which the raw material is pyrrhotite or hydrogen sulfide, the maximum concentration of sulfur trioxide after conversion is about 7.0%. No more than 25% of the total sulfur trioxide content of gas can then be absorbed in the 40% tower, whereas on a full strength brimstone gas of 10.5% SO<sub>3</sub> content nearly 50% of the sulfur trioxide is available for production of 40% oleum. If it is desired to produce 45% oleum, the sulfur trioxide available from the 10.5% gas drops to 25% while no oleum of this strength can be produced from the 7.0% gas.

The sulfur trioxide content of the gas leaving the contact converters can be more than doubled by installing, ahead of the strong oleum tower, a stripping tower in which the sensible heat of the gas leaving the final converter or transferer is utilized to vaporize sulfur trioxide from 20 to 30% oleum fed to the stripper. The residue from the stripper, usually about 5% oleum, is returned to the intermediate oleum tower. By this procedure (14) sulfur trioxide can be absorbed in the 40% tower in excess of the amount present in the original converted gas. It also makes possible the production of oleum as strong as 60% by direct absorption, although, when utilizing a 7.0% gas, this would require an absorption train comprising a stripper, 60% tower, 50% tower, 30% tower, and final 99% absorber.

Higher strength oleum is produced by heating strong oleum and absorbing the vaporized sulfur trioxide in an additional body of strong oleum with concurrent cool-

ing; the weak oleum residual from the boiler being returned to the oleum tower for fortification. The higher the strength of the oleum employed for absorption of the vaporized sulfur trioxide, the lower the cost of production. Sulfuric anhydride (sulfur trioxide) is produced in a similar manner by cooling and condensing the sulfur trioxide vaporized in the boiler. See p. 501.

Since production of oleum necessitates bringing gas from the final converter or transferrer into contact with acid much below the condensation point, the result is the chilling of the gas with formation of sulfuric mist that will cause a visible exit from the final absorber. The higher the strength of the oleum being produced, the lower the temperature of the circulating acid, and the worse the exit. When the stripper is included in the oleum system, the weak oleum at the base of the stripper at its first contact with the entering gas is raised to as high as 275°F., with the result that gas is gradually cooled through the major portion of the condensation range. This materially reduces formation of mist with corresponding reduction in visible exit from the absorber stack.

The oleum coolers incorporated in the acid circulation system are steel, and the same principle applies as in the case of absorbing tower coolers. Pumps and circulating lines must also be steel.

**Nitrification of Oleum.** Due to the high freezing point of oleum of the higher strengths, particularly 40% oleum employed so extensively in production of high explosives, it is customary to use nitric acid as an anti-freeze. Addition of 6% by weight of 96%  $\text{HNO}_3$  to 40% oleum will depress the freezing point from 75 to  $-11^\circ\text{F}$ . The nitric acid is added continuously to the product leaving the 40% system, and as the addition produces considerable temperature rise, this provides a means of effecting automatic regulation of the nitric acid content. Where end use prohibits the use of nitric acid, a hot shed must be provided to thaw oleum frozen in transit.

#### WET GAS SYSTEM

Between January, 1944, and July, 1945, the General Chemical Division, Allied Chemical & Dye Corporation, built seven sulfuric plants under contract to the Defense Plant Corporation, with a combined capacity of 365,000 net tons of sulfuric acid per year. These greatly simplified units, designed for operation on brimstone, eliminated the drying of air, gas, or sulfur and the conventional heat transfer vessels for removing heat of conversion.

Brimstone was charged to a solid-feed sublimizer, without prior drying or melting. Undried air was supplied to the sublimizer and subsequent combustion chamber, and the wet sulfur dioxide gas, after cooling to about 825°F., was passed through a hot gas filter and then entered the first converter. The initial gas strength varied from about 11.5 to as high as 13.7%  $\text{SO}_2$ , which would leave only 7.3%  $\text{O}_2$ —clearly not enough for conversion. Three stages of vanadium catalyst were employed. Interstage cooling of the gas was by dilution with cold, undried air, rather than by coolers. This gave a very simple temperature control, and the problem of corrosion of the coolers was eliminated by eliminating the coolers. The ultimate gas concentration at the outlet of the final converter was about 7%  $\text{SO}_3$ . This figure is virtually independent of the initial gas strength, since the temperature rise with the higher gas strength necessitated the use of more dilution air between stages.

Gas leaving the final converter was carried through an insulated flue to a packed tower operating as a combined condenser and absorber. Due to the high moisture

content of gas which, varying with season and geographic location of plant, ran from 1.0 to 2.5%  $\text{H}_2\text{O}$  by volume, it was necessary to operate with acid in first contact with gas at a temperature as high as 325°F. to avoid formation of objectionable amounts of sulfuric acid mist. Oleum was produced in one of these plants, the remainder producing 99% acid to be used as diluent in other oleum systems.

#### SPECIAL PURPOSE PLANTS

**Acid Sludge Decomposition.** Acid sludges produced in treating petroleum distillates with sulfuric acid vary widely in composition and are broadly classed as nonlube and lube sludges. Most refineries hydrolyze the light nonlube sludges, effecting an incomplete separation of acid tars from the weak impure acid. The acid is then concentrated to about 80%  $\text{H}_2\text{SO}_4$  and mixed with strong acid, or fortified with sulfur trioxide for re-use, but it has a high organic content which may run to 8–10% expressed as carbon. The heavy lube sludges of low acidity have usually been disposed of by burning, either under the boilers or in a special incinerator.

Where clean acid is desired, it is necessary to decompose the sludge, and this can be effected in the mechanical furnace employed for roasting ore, but if handled in any volume the oxygen consumed in formation of water and carbon dioxide results in a dilute sulfur dioxide gas that imposes a heavy penalty on the associated acid plant.

Several plants have been built for the express purpose of utilizing the higher acidity sludges with a titratable acidity of 45 to 55% for production of clean acid. The sludges are subjected to thermal decomposition in a brick-lined rotary kiln, equipped at the discharge end with one or more heavy iron bars to granulate the coke which may amount to 35–45% by weight of sludge charged. The decomposition is effected by supplying the kiln with hot products of combustion of low oxygen content from a fuel-fired furnace. The required heat has also been provided by charging into the kiln hot coke obtained by burning a portion of the by-product in a separate kiln or furnace.

Since the evolved gases contain varying amounts of condensable hydrocarbons, these must be condensed by cooling. This is accomplished by direct contact with water recirculated over towers in a closed circuit with external cooling. The gas is then diluted with air and raised to about 1500°F. for combustion of any uncondensed hydrocarbons and all noncondensable hydrocarbons, and, after passage through a heat exchanger, is subjected to a second cooling in a system similar to the first. The gas, which contains about 7%  $\text{SO}_2$ , passes through a Cottrell and then enters the blower which forces it through a standard contact unit equipped with heat exchangers similar to a wet purification unit.

A modified Mannheim furnace equipped with a double muffle has also been employed. This avoids the dilution of the gas with carbon dioxide and nitrogen, but the evolved sulfur dioxide gas must be freed of condensable and noncondensable hydrocarbons, and dried before delivery to the contact plant.

Where sulfuric acid is used as the catalyst in the alkylation process, the 99% acid is diluted by absorption of hydrocarbons and various by-products. In practice, the acid in circulation is maintained at from 88 to 92% titratable acidity by continuous addition of fresh 99% acid, with discard of an equivalent volume of contaminated acid. This alkylate discard, which usually averages from 5 to 8% organic, expressed as carbon, is decomposed by spraying into a combustion chamber in which the heat deficiency is made up by use of other fuel, or, if additional production is required, molten

or vaporized brimstone can be substituted in whole or in part. Since the decomposition is effected at about 1800°F. in the presence of an excess of oxygen, all organic matter is completely burned and the gas can be handled in a standard wet purification acid unit, or cooled by direct contact with water, passed through a Cottrell for removal of mist, and dried prior to admission to a contact unit containing heat exchange equipment. The impure acid recovered by hydrolysis of nonlube sludges, can, after concentration, be similarly decomposed.

The acid recovered in the production of explosives, which contains up to about 0.25% nitrobodyes, can be decomposed at about 1800°F. in a low-oxygen atmosphere by hot products of combustion from a fuel-fired furnace. The decomposition can also be effected by combustion of brimstone.

**Sulfate Conversion Unit.** Several plants have also been built for processing the waste liquors from the titanium pigment industry, which contain from 9 to 15%  $\text{H}_2\text{SO}_4$  and from 10 to 4%  $\text{FeSO}_4$ . The acid liquors are fed into a fuel-fired, brick-lined rotary kiln together with a portion of the iron oxide by-product for neutralization of the free acid. As the material progresses through the kiln, it passes through a pasty stage into a solid, which is granulated by tumbling irons and is eventually discharged in the form of  $\text{FeSO}_4 \cdot \text{H}_2\text{O}$ ; the waste gases being discharged to the atmosphere. The ferrous sulfate monohydrate is then charged into a second similar fuel-fired kiln, after admixture with powdered coal, or a mixture of coal and pyrite ore. Here the sulfate is decomposed and the pyrite oxidized resulting in by-product ferric oxide, part of which is recycled to the first kiln. Gas leaving the decomposing kiln is passed through a hot Cottrell for removal of dust, and is then cooled and scrubbed. The gas, containing about 7%  $\text{SO}_2$ , is then sent to a contact unit equipped with heat exchangers.

The waste titanium liquors have also been subjected to vacuum concentration for recovery of the free acid for re-use in the process; the ferrous sulfate is either crystallized out as the heptahydrate or salted out as the monohydrate by regulating the acid concentration.

A similar type of plant has been proposed for processing the huge volumes of pickle liquor discarded by the steel mills. These liquors also contain free  $\text{H}_2\text{SO}_4$  and  $\text{FeSO}_4$  in varying amounts, but are generally more dilute than the titanium waste liquors, and the economics are consequently less favorable. The ferrous sulfate can be decomposed by heat alone, or by feeding together with sulfide ore into an ore burner in which the temperature is maintained above the dissociation point of sulfur trioxide.

In a recent proposal, the ferrous sulfate monohydrate would be mixed with fuel and decomposed on a Dwight-Lloyd sintering machine. This would produce a dilute impure sulfur dioxide gas that would have to be purified and dried prior to delivery to an associated acid plant.

The selection and use of such special type plants is not, in most instances, approached from the standpoint of producing acid under commercially competitive conditions. Rather, they are intended to solve a waste disposal problem, thereby avoiding air and stream pollution.

### Economic Aspects

U.S. production of sulfuric acid has increased from 1,680,000 net tons in 1911 to 13,339,000 net tons in 1952, an increase of 694% in this period of 41 years. This is shown graphically in Figure 19, with a breakdown since 1920 between chamber and

contact production, and in Figure 20, with a breakdown among raw materials. It is of interest to note that since 1931 the curves for sulfur as raw material, and contact production, parallel the curve for total production. Since 1950, shortage of brimstone in conjunction with increased price has resulted in a return to the use of ore in some plants, and this trend can be expected to continue.

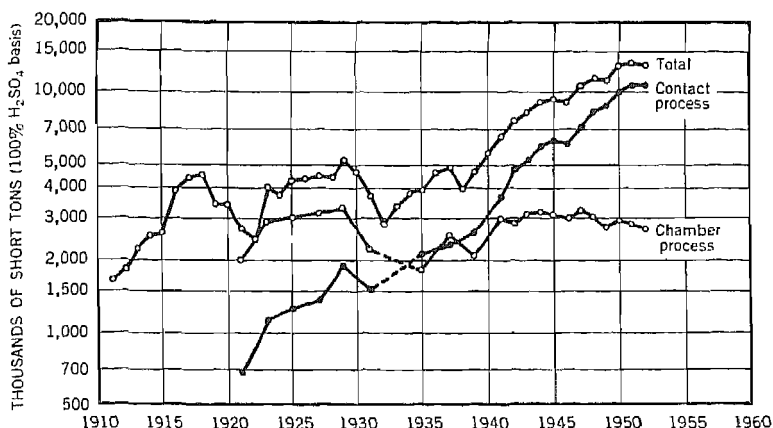


Fig. 19. U.S. production of sulfuric acid, by processes. (Source: *Chemical Economics Handbook*, Stanford Research Institute.)

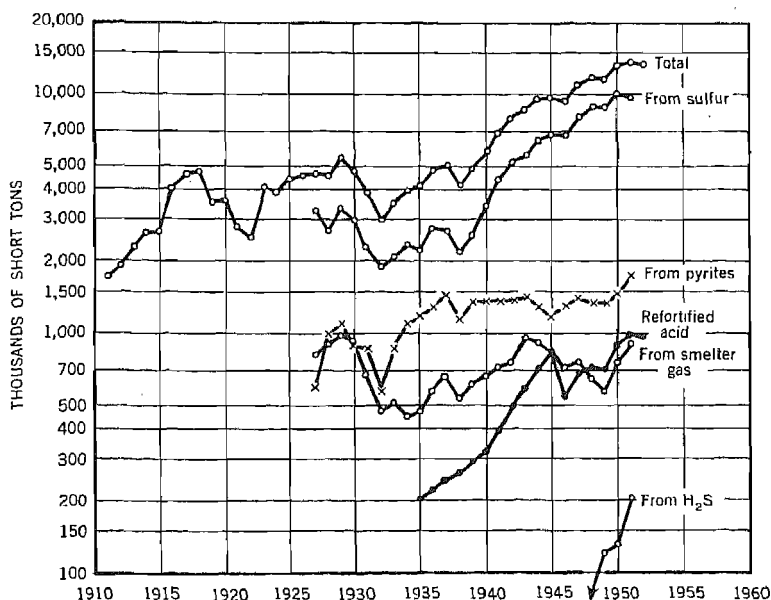


Fig. 20. U.S. production of sulfuric acid, by raw materials. (Source: *Chemical Economics Handbook*, Stanford Research Institute.)

U.S. consumption in 1952, 14,700,000 net tons, exceeded the virgin acid production by 1,301,000 net tons, which represents recovered acid.

The average yearly wholesale price, basis 66°Bé., is plotted in Figure 21, illustrating the price stability which was upset only by the acute shortage that developed

during the first World War. The present moderate up-trend reflects primarily increased raw material costs.

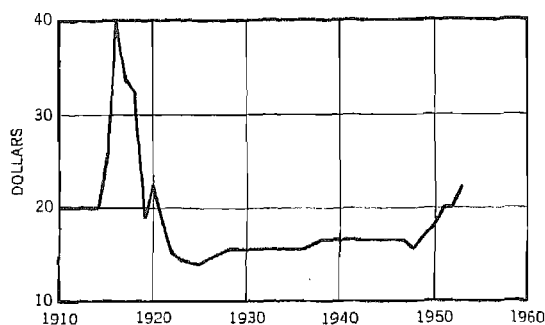


Fig. 21. Price of sulfuric acid.

Distribution of virgin acid production for 1951 by States and Divisions, as reported by Bureau of the Census, Industry Division, is given in Table VI. Production of sulfuric acid in the United Kingdom, Australia, Canada, Ireland, and some other European countries where available is given in Table VII.

TABLE VI. Production in Net Tons of New Acid in 1951, by Divisions and States.

New England <sup>a</sup> .....	210,324
New York and New Jersey .....	1,348,451
Pennsylvania .....	808,334
Illinois .....	1,073,223
Indiana .....	464,896
Ohio .....	654,321
North Central—other <sup>b</sup> .....	798,472
Alabama .....	298,404
Florida .....	535,719
Georgia .....	247,307
North Carolina .....	160,087
South Carolina .....	206,779
Virginia .....	549,918
Kentucky and Tennessee .....	835,310
Texas .....	947,916
Delaware and Maryland .....	1,340,009
Louisiana .....	435,335
South—other <sup>c</sup> .....	489,988
West <sup>d</sup> .....	984,075
<i>Total</i> .....	12,388,868

<sup>a</sup> Includes Maine, Rhode Island, Massachusetts, and Connecticut.

<sup>b</sup> Includes Missouri, Michigan, Wisconsin, Iowa, and Kansas.

<sup>c</sup> Includes West Virginia, Mississippi, Arkansas, and Oklahoma.

<sup>d</sup> Includes Arizona, California, Colorado, Montana, Utah, Washington, and Wyoming.

### Analysis and Specifications

For 60° and 66°Bé. strengths, determination of the specific gravity by means of a Baumé hydrometer is generally employed. Such hydrometers should be graduated at 60°F. For extreme accuracy the 66°Bé. hydrometer can be obtained with a 6-in.



TABLE VII. Production in Net Tons of Sulfuric Acid in 1952 in Europe and Units of British Commonwealth.

Australia.....	734,227
Canada.....	816,270
United Kingdom.....	1,505,473
Ireland.....	85,580
Germany (West).....	1,851,190
Italy.....	1,568,600
France.....	1,316,920
Belgium-Luxembourg.....	941,490
Netherlands.....	637,340
Sweden.....	349,800
Portugal.....	203,060
Denmark.....	181,060
Switzerland.....	123,640
Greece.....	65,450
Austria.....	21,560
Germany (East).....	276,000
Yugoslavia.....	39,194

stem graduated over the range of 63.0° to 66.5°Bé. The acid should always be tested at about room temperature and a temperature correction applied of 0.026°Bé. for 1°F. on 60°Bé. acid and 0.0235°Bé. for 1°F. on 66°Bé. acid. The U.S. Bureau of Standards will check instruments and supply a chart noting corrections to be applied, and these standardized instruments can then be employed to standardize the working instruments.

For acid stronger than 66°Bé., the strength is determined by titration of a weighed sample with standard alkali. Since oleum reacts violently with water, the sample should be weighed in a "snake" tube of Pyrex with a capillary point. After weighing, while holding the index finger over the open end of the tube, the point is immersed in a casserole of water and the oleum permitted to run slowly into the water, and the empty tube is finally flushed with distilled water. For extreme accuracy, a water-jacketed buret should be employed to avoid temperature changes.

Methods for determination of the impurities in sulfuric acid are fully covered in a Federal Specification (2) established by the General Service Administration for all agencies. Although applying specifically to electrolyte acid, it covers all impurities except lead, which is determined colorimetrically, using sodium sulfide to produce a brown coloration.

Standard commercial strengths of sulfuric acid are: 60°Bé. (77.67%), 66°Bé. (93.19%), 99%  $\text{H}_2\text{SO}_4$ , and 20, 40, and 65% oleum. Electrolyte acid for storage batteries is supplied at any strength between sp.gr. 1.200 (27.24%) and sp.gr. 1.835 (93.19% or 66°Bé.) to meet customer specification. Chemically pure acid is supplied at a strength of 95-96%  $\text{H}_2\text{SO}_4$  to meet A.C.S. specification.

No product specifications have been established other than the purchase specifications issued by the Armed Services and other governmental agencies, covering a few impurities. However, as a result of competitive conditions within the industry, the specifications as given in Table VIII are generally applicable to commercial grades.

Many rayon producers specify an iron content of 0.005% Fe for commercial 66°Bé. and for electrolyte acid of 1.835 sp.gr., the iron specification is reduced to 0.0042% Fe with the following added maximum permissible impurities: Pt, 0.00001%; Mn,

TABLE VIII. Product Specifications—Commercial Grades.

Max. impurity	60° Bé., 66° Bé., 99% H <sub>2</sub> SO <sub>4</sub>	20 Oleum, % 40 65
HCl, %	0.0005	0.0005
HNO <sub>3</sub> , %	0.0005	0.0005
SO <sub>2</sub> , %	0.015	0.015, 0.015, 0.07
NH <sub>3</sub> , %	0.001	—
As <sub>2</sub> O <sub>3</sub> , %	0.00005	0.00005
Fe, %	0.015	0.02
Pb, %	0.005	0.005
Non.vol., %	0.05	—
Color	Very slight yellow tint	Gray
Turbidity	Slightly cloudy	Cloudy

0.00002%; Sb, 0.0001%; Ni, 0.0001%; Se, 0.002%; Zn, 0.004%; Cu, 0.005%; acid colorless and clear.

The commercial grades of sulfuric acid and oleum are shipped in steel drums (returnable), tank trucks, tank cars, and tank barges. In addition, acid below the monohydrate is shipped in glass carboys (returnable). Electrolyte quality 1.835 sp.gr. is shipped in specially prepared steel tank trucks, tank cars, and glass carboys. Weaker grades of electrolyte acid and C.P. sulfuric are shipped in glass containers only.

All shipments must be protected by the "white label" for corrosive liquids. The labels must be removed from returning empties. All containers must comply with the respective specifications of the Interstate Commerce Commission and must be marked to show such compliance. The large producers own their own fleets of tank trucks, tank cars, and tank barges and there are several tank car operating companies from whom cars can be leased.

### Materials of Construction and Safety

Lines for handling 60°Bé. acid or under should be of lead. For handling 66°Bé. and 99% acid, cast iron lines are less subject to corrosion than wrought iron, but are not suited to withstand shock. It is, therefore, customary to employ heavy cast-iron flanged pipes and fittings for circulating lines and wrought-iron lines for delivery to storage. Steel lines are employed for all strengths of oleum. Steel tanks are used for storage and transportation of all strengths of acid 60°Bé. and above, although corrosion is materially higher on 60°Bé. acid than at higher strengths, particularly at higher temperatures. Lead must be used for acid weaker than 60°Bé.

### Health and Safety

Sulfuric acid is injurious to the skin, mucosa, and eyes. Dangerous quantities of hydrogen may develop in reactions between weakened acid and metals. Sulfuric acid reacts vigorously with organics and reducing agents. It is a strong dehydrating agent.

Those engaged in handling sulfuric acid should obtain information on safe handling and use. Suggested literature, available from Manufacturing Chemists' Association, Inc., 246 Woodward Building, 15th and H Streets, N.W., Washington 5, D.C., includes:

## M.C.A. Safety Pamphlets—Sulfuric Acid

C- 3	Carboy bottle, 13 gal. (I.C.C. Spec. 1A)
D-31	Steel drums (I.C.C. Spec. 5A)
SD-20	Sulfuric acid
TC- 1	Tank cars (I.C.C. Spec. 103A)

Much help in promulgating a program for safe handling of acid may be obtained from manufacturers and safety engineers familiar with chemical operations. Containers as received should be carefully inspected and set aside for special handling if defects are found. Manufacturers' recommendations for storage and unloading should be strictly followed. To prevent accumulation of hydrogen in drums, they should be periodically vented. Special precautions are necessary if a tank is to be entered for repair or cleaning. Workers responsible for handling sulfuric acid should wear protective clothing and equipment as described in M.C.A. SD-20. Safety showers, protected against freezing and with deluge heads, should be readily available.

Sulfuric acid has the peculiar property of plugging up lines due to formation of iron or lead sulfates. In dismantling lines and equipment, the assumption should always be made that a spray of acid may occur, and necessary precautions should be taken.

As a general rule, acid should never be diluted by addition of water. The acid should always be poured into the water and this is particularly important in the case of strong acid. Since the dilution is accompanied by a considerable evolution of heat, it should never be carried out in a heavy glass vessel unable to withstand sudden temperature changes.

The plant should be provided with a well-equipped hospital room, or first-aid station, under the supervision of a trained nurse. Where the nurse is not provided, selected members of the office or laboratory force should be adequately trained to render first aid while awaiting arrival of doctor or ambulance. A continuing program to teach and enforce safe work habits is essential to safe handling of sulfuric acid.

### Uses

Table IX gives the uses of sulfuric acid.

The fertilizer industry is the largest consumer of sulfuric acid, production of superphosphates accounts for about 26% of the total acid consumption, chiefly from captive plants, and to this must be added another 8% consumed in the production of ammonium sulfate. The chemical industry is the second largest consumer, accounting for approximately 20% of total acid consumption. Some of the more important uses are the production of phosphoric acid by the wet process, aluminum sulfate used extensively for water purification and in manufacture of paper, and the rapidly growing petrochemical industry.

The petroleum industry is the third largest consumer, accounting for about 12% of total acid production, of which approximately 60% is used in the relatively new alkylation process for production of alkylate of high-octane blending power. Sulfuric acid is also used in refining of petroleum distillates for removal of sulfur and gum-forming compounds. Acid used for these purposes is recoverable as a waste acid or acid sludge that may be separated by hydrolysis into an impure acid, or decomposed and converted into clean fresh acid as noted under "Special Purpose Plants."

Among other important industries consuming large tonnages of sulfuric acid are titanium pigments, steel-pickling, rayon, dyes and intermediates, and detergents.

TABLE IX. Sulfuric Acid End-Use.

End-use	1951 Consumption, net tons H <sub>2</sub> SO <sub>4</sub> (000 omitted)
Aluminum sulfate.....	413
Ammonium sulfate.....	1,218
Aviation gasoline.....	952
Other petroleum products.....	673
Boric acid.....	34
Chemicals (not otherwise classified).....	1,959
Chromium chemicals.....	87
Copper sulfate.....	46
Dyes and intermediates.....	309
Food testing and processing.....	15
Hydrogen chloride.....	170
Hydrofluoric acid.....	131
Industrial explosives.....	122
Insecticides.....	137
Iron and steel pickling.....	975
Light oil refining (coke oven).....	75
Lead, zinc, and titanium pigments.....	1,280
Other metallurgical.....	183
Medicinals.....	33
Nonferrous metal pickling.....	22
Petroleum catalysts and silica gel.....	148
Petroleum sulfonates.....	153
Phenol.....	144
Rayon and cellophane.....	722
Rubber (including synthetic).....	138
Storage batteries.....	80
Superphosphates.....	3,850
Synthetic detergents.....	214
Tall oil.....	46
Textile finishing.....	34
Miscellaneous.....	326
<i>Total</i> .....	14,689
Virgin acid production.....	12,385
Indicated use of recovered acid.....	2,304

## Bibliography

- (1) Fairlie, A. M., *Sulfuric Acid Manufacture*, Reinhold, N.Y., 1936.
- (2) Federal Specification 05-801, Aug. 1952, Superintendent of Documents, Washington.
- (3) I.C.T., Vol. III, 1928, p. 56.
- (4) *Trans. Soc. Chem. Ind. London*, 257 (1921).
- (5) Knietzsch, K., *Ber.*, **34**, 4069 (1902).
- (6) Mellor, Vol. X, 1930, pp. 353, 391, 410.
- (7) Miles, F. D., *Manufacture of Sulphuric Acid (Contact Process)*, *Lunge Series on the Manufacture of Acids and Alkalis*, Vol. 4, A. C. Cumming, ed., Van Nostrand, N.Y., 1925, p. 348.
- (8) Miles, F. D., Niblock, H., and Smith, D., *Trans. Faraday Soc.*, **40**, 287 (1944).
- (9) Miles, F. D., Niblock, H., and Wilson, G. L., *Trans. Faraday Soc.*, **36**, 350 (1940).
- (10) Parkes, J. W., *Concentration of Sulphuric Acid*, *Lunge Series on the Manufacture of Acids and Alkalis*, Vol. 3, A. C. Cumming, ed., Van Nostrand, N.Y., 1924.
- (11) Perry, J. H., *Chemical Engineers Handbook*, 3rd ed., McGraw-Hill, N.Y., 1950, pp. 234, 168, 169. Table IV courtesy McGraw-Hill Book Company, Inc.
- (12) Socolik, A. S., *Z. physik. Chem.*, **158A**, 305 (1932).

- (13) Wyld, W., *Raw Materials for the Manufacture of Sulphuric Acid, and the Manufacture of Sulphur Dioxide*, Lunge Series on the Manufacture of Acids and Alkalis, Vol. 1, A. C. Cumming, ed., Van Nostrand, N.Y., 1923, pp. 3, 379.
- (14) Wyld, W., *Manufacture of Sulphuric Acid (Chamber Process)*, Lunge Series on the Manufacture of Acids and Alkalis, Vol. 2, A. C. Cumming, ed., Gurney and Jackson, London, 1924, p. 144.
- (15) Zeisberg, F. C., *Chem. & Met. Eng.*, **27**, 22 (1922); *Trans. Am. Inst. Chem. Engrs.*, **14**, 1 (1922).
- (16) U.S. Pat. 1,384,566 (July 12, 1921), H. F. Merriam (to General Chemical Co.).
- (17) U.S. Pat. 2,394,426 (Feb. 5, 1946), B. M. Carter (to General Chemical Co.).
- (18) U.S. Pat. 1,371,004 (March 8, 1921), F. Slama and H. Wolf (to General Chemical Co.) (Reissue 19,282, August 21, 1934).

B. M. CARTER

### Sulfur Trioxide

Sulfur trioxide (sulfuric anhydride),  $\text{SO}_3$ , formula weight 80.06, although manufactured for many years by the chamber process and more recently by catalytic oxidation of sulfur dioxide for use in production of sulfuric acid and oleum, was formerly used only at the point of manufacture in the form of converter gas or as a liquid stored for very limited time in a warm storage tank. Its strong tendency to polymerize to the more stable solid forms prevented it from being shipped. In a few isolated cases, it was shipped as oleum from which it was recovered by distillation, but serious drawbacks such as high freight costs and formation of large quantities of residual acid made this impractical. Since most organic sulfonations are conducted at locations where sulfuric acid is not manufactured, it followed that sulfur trioxide was of little interest for such purposes under these circumstances.

It has long been recognized, however, that in theory sulfur trioxide is a most efficient reagent for a wide variety of organic sulfonations and sulfations (see *Sulfonation and sulfation*). With sulfuric acid (or oleum) the large excess of reagent used is lost to the process. Rapidly expanding production of sulfonates during and after World War II has resulted in larger volume of spent sulfuric acid, which has created serious disposal problems, particularly in the face of more drastic legislation governing effluent disposal. In some processes, special measures must be adopted to distil out water formed during the reaction. With chlorosulfonic acid, by-product hydrogen chloride is liberated which is not only nonproductive, but often a serious disposal problem in itself. Since the use of sulfur trioxide could simplify or eliminate these problems, much could be gained by the development of inhibitors that would prevent or retard polymerization and permit shipment of the liquid as an ordinary article of commerce from point of manufacture to consumer. Research in this direction was successful (10-14) and one such product was introduced in 1947 under the trade name Sulfan (8). Since then, liquid sulfur trioxide has become an important basic industrial chemical.

### PROPERTIES

Liquid sulfur trioxide is a colorless liquid, b.p.  $44.8^\circ\text{C}$ ., specific heat ( $25\text{--}35^\circ\text{C}$ .) 0.77, heat of vaporization 130.7 cal./g.,  $t_c$   $218.3^\circ\text{C}$ .,  $P_c$  83.8 atm., density see Figure 1, viscosity see Figure 2. For heat of dilution see Figure 3, whose use is explained below by giving the solution of two problems. See also p. 466.

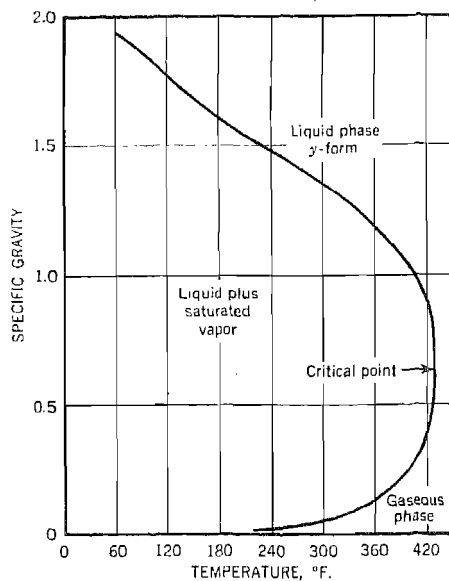
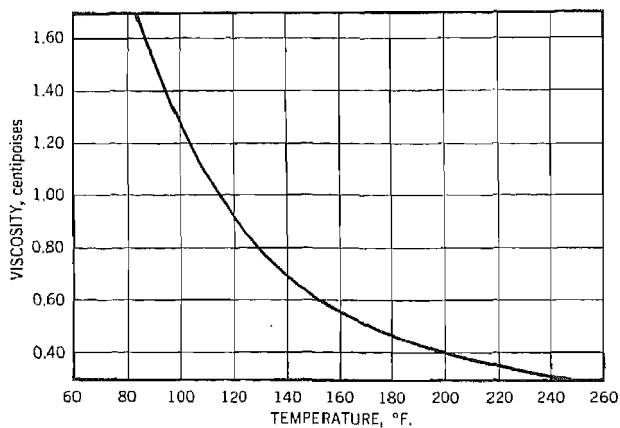
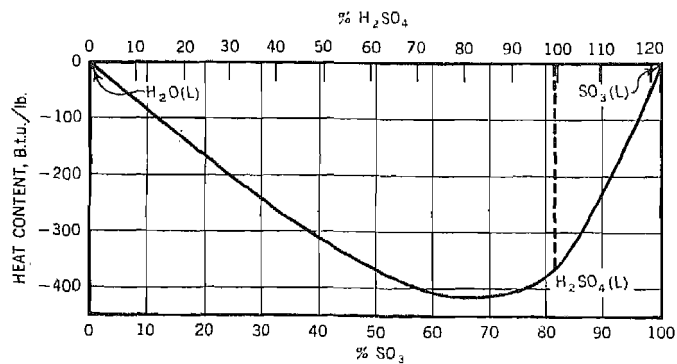


Fig. 1. Specific gravity of sulfur trioxide.



*Courtesy General Chemical Division, Allied Chemical & Dye Corporation.*

Fig. 2. Viscosity of sulfur trioxide.



*Courtesy General Chemical Division, Allied Chemical & Dye Corporation.*

Fig. 3. Relative heat content of sulfuric acid, oleum, and sulfur trioxide at 30°C.

Problem 1: Find the heat evolved when 1 lb. 40% sulfuric acid is mixed with 4 lb. 75% sulfuric acid.

1. Mixture produced:

$$5 \text{ lb. of } \frac{40\% \times 1 \text{ lb.} + 75\% \times 4 \text{ lb.}}{5 \text{ lb.}} = 68\% \text{ acid}$$

2. Heat content of components from graph:

$$(1 \text{ lb.})(-260 \text{ B.t.u.}) + (4 \text{ lb.})(-409 \text{ B.t.u.}) = -1896 \text{ B.t.u.}$$

3. Heat content of product:

$$(5 \text{ lb.})(-391 \text{ B.t.u.}) = -1955 \text{ B.t.u.}$$

4. Heat evolved by difference:

$$-1896 \text{ B.t.u.} + (-1955 \text{ B.t.u.}) = +59 \text{ B.t.u.}$$

Problem 2: Find the heat evolved when 1 lb. 35% sulfuric acid is mixed with gaseous sulfur trioxide to make 100% sulfuric acid.

1. Weight of sulfur trioxide required per lb. 35% sulfuric acid (from graph):

$$\frac{81.6\% \text{ SO}_3 - 28.6\% \text{ SO}_3}{100\% \text{ SO}_3 - 81.6\% \text{ SO}_3} = \frac{53.0}{18.4} = 2.88 \text{ lb.}$$

2. Heat content of components (including heat of condensation of sulfur trioxide, 235 B.t.u./lb.):

$$(1 \text{ lb.})(-230 \text{ B.t.u.}) + (2.88 \text{ lb.})(235 \text{ B.t.u.}) = 447 \text{ B.t.u.}$$

3. Heat content of product:

$$(3.88 \text{ lb.})(-362 \text{ B.t.u.}) = -1401 \text{ B.t.u.}$$

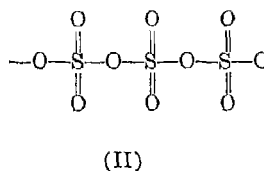
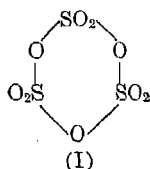
4. Heat evolved by difference:

$$447 \text{ B.t.u.} - (-1401 \text{ B.t.u.}) = 1848 \text{ B.t.u. evolved}$$

The physical behavior of solid sulfur trioxide is complex and not fully understood. On cooling, ice-like crystals of the  $\gamma$ -form are obtained. This has a melting point of about  $16.8^\circ\text{C}$ . If traces of sulfuric acid are present, the feathery  $\beta$ -form tends to develop, m.p.  $32.5^\circ\text{C}$ . This formation can be prevented by adding phosphorus pentoxide (7); sulfur, tellurium, carbon tetrachloride, and phosphorus (V) oxychloride have also been suggested as inhibitors (5). The addition of very small quantities of boron oxide, other boron compounds, or antimony pentachloride or pentafluoride, as inhibitors, has been patented (12,13,14). The  $\beta$ -form may undergo a further conversion to the asbestos-like  $\alpha$ -form, m.p.  $62.3^\circ\text{C}$ . (The designations of these three forms have been applied differently (9).)

The properties of the solids in some cases may depend on the history of the sample, and it appears that a number of nonequilibrium solids of varying properties can be obtained. The two lower-melting forms are metastable with respect to the highest-melting form.

The  $\gamma$ -form is believed to have a trimeric structure (I) and the  $\beta$ - and  $\alpha$ -forms a linear structure (II); in the  $\alpha$ -form the chains are joined to one another in a layered structure (see also *Sulfur compounds—structure*). Thus the order  $\gamma$ ,  $\beta$ ,  $\alpha$  is the order of increasing complexity.



Some properties of the three forms are given in Table I.

TABLE I. Properties of Solid Sulfur Trioxide.

Property	$\gamma$	$\beta$	$\alpha$
Equilibrium m. p., °C.	16.8	32.5	62.3
Heat of fusion, cal./formula wt. $\text{SO}_3$	1,800	2,900	6,200
Heat of sublimation, cal./formula wt. $\text{SO}_3$	11,900	13,000	16,300
Vapor pressure, mm.			
0°C.	45	32	5.8
25°C.	433	344	73
50°C.	950	950	650
75°C.	3,000	3,000	3,000

#### MANUFACTURE

Liquid sulfur trioxide is manufactured by distillation from strong oleum and condensation. The still bottoms are generally returned to the absorption towers as 10% oleum. Condenser temperature must be closely controlled to prevent freezing on the condenser surface. Successful and trouble-free operation of either the manufacturing plant or facilities utilizing it depends entirely upon eliminating even traces of moisture contamination and maintaining equipment, lines, and valves above 30°C. As it is virtually impossible to eliminate moisture completely, unstabilized sulfur trioxide has an extremely limited shelf life. The vapor pressure being quite high, vent exits are generally scrubbed with strong or absorbing strength (98–99.5%) sulfuric acid before discharge.

**Materials of Construction.** Steel is entirely satisfactory for use in construction of the still, condenser, storage tanks, and piping. Although carbon steel is suitable for pumps and valves, experience has indicated that stainless steel types such as 316, 347, and FA-20 (Carpenter 20, Durimet 20) are more desirable from the standpoint of maintenance and operation. Monel and Ni-Resist have also been successfully used. Cast iron, brass, or bronze should be avoided. Preferred gasketing and packing material is tetrafluorethylene (Teflon) or fluorothene (chlorotrifluoroethylene, Kel-F or CF-3). See Vol. 11, pp. 687, 691. Hard asbestos may be substituted in an emergency. Rubber, neoprene, polyethylene, and other organic gasket material should not be used as gasketing and packing material.

**Containers.** Shipment of liquid sulfur trioxide is approved by the I.C.C. only in stabilized form. Small quantities, under 1 gallon each per unit, should be packaged in heat-resistant-type glass ampules protected by incombustible absorbent material and shipped in I.C.C. specification 15A, 15B, 15C, 16A, or 19A wooden boxes. Larger amounts not exceeding 55 gallons per unit may be packed in I.C.C. 5A or 5C returnable or 17F single-trip steel drums. Tank-car quantities may be shipped in I.C.C. specification 103A or 103A-W cars equipped with external heater coils. Shipments must bear I.C.C. white label for corrosive liquids.

**Safety and Precautions.** The fumes of sulfur trioxide, although highly toxic, are also extremely irritating and unbreathable. Consequently, although maximum concentration that may be tolerated for prolonged exposure (8 hours) is reported as 2 p.p.m., and 10 p.p.m. will kill most animals in a few minutes (1,4), it is highly unlikely



that one would remain in an area of such concentration unless he were unconscious or trapped. It is for this reason that so few accidents are recorded. Adequate ventilation and necessary safety respiratory equipment should be provided.

The liquid is strongly acidic and corrosive to the skin. Reaction with clothing and organic materials is vigorous. In case of contact with skin or eyes, flooding with large quantities of running water should be continued for at least fifteen minutes. For eye or serious skin burns, medical attention should be obtained immediately. All personnel handling sulfur trioxide should be provided with adequate protective equipment, including neoprene gloves, full face shields, and safety glasses, neoprene or rubber shoes, and preferably rubber clothing, although certain of the synthetic fiber clothes may be substituted.

Sulfur trioxide is a powerful oxidizing and dehydrating agent and will set fire to such material as excelsior and sawdust upon contact. It reacts violently, almost explosively, with water to form sulfuric acid. In case of spillage, it should be neutralized with soda ash or lime or absorbed in sand, earth, or other inert material before removal. Small amounts may be vaporized with dry steam and the residue neutralized and flushed with water.

Polymerized material, if small in amount and if local ordinances permit, may be buried in the plant dump. Larger quantities should be carefully dissolved with as high a strength oleum as is available. Agitation must be provided to prevent stratification and build-up of large quantities of the weaker oleum which might subsequently mix with vigorous heat release. Cooling should be provided to facilitate the disposal process.

#### USES

Since commercial introduction of stabilized sulfur trioxide, its uses have expanded rapidly. Detergents (both household and industrial), wetting agents, emulsifying agents, lubricant additives, resorcinol, and other products are being produced with this material. It reacts with most organic compounds and there are many potential uses involving reaction with various alcohols, aromatic and aliphatic carboxylic acids, and aromatic hydrocarbons and their derivatives including salicylic acid, and acetanilide (2,3,6).

The disadvantages of sulfur trioxide may be high heat of reaction and greater viscosity of reaction mixture, as well as the special handling and storage techniques. Its advantages are: avoidance of spent sulfuric acid formed in oleum or acid sulfonation, elimination of by-product hydrogen chloride formed when using chlorosulfonic acid for sulfation, reduced shipping weight, reduced reactor volume, faster rate of throughput resulting from elimination of digest period, lower inorganic sulfate content of final product, and higher reactivity in difficult sulfonations.

#### Bibliography

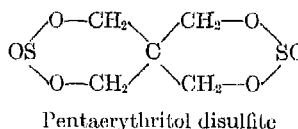
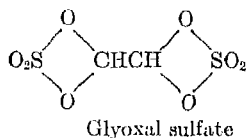
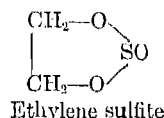
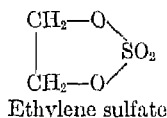
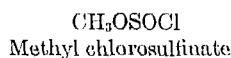
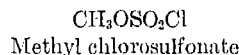
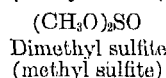
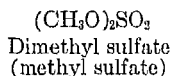
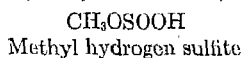
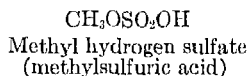
- (1) Brookes, V. J., and Alyea, H. N., *Poisons, Their Chemical Identification and Emergency Treatment*, Van Nostrand, N.Y., 1946, p. 160.
- (2) Gilbert, E. E., and Jones, E. P., *Ind. Eng. Chem.*, **45**, 2041 (1953).
- (3) Gilbert, E. E., Veldhuis, B., Carlson, E. J., and Giolito, S. L., *Ind. Eng. Chem.*, **45**, 2065 (1953).
- (4) Jacobs, M. B., *The Analytical Chemistry of Industrial Poisons, Hazards, and Solvents*, 2nd ed., Interscience, N.Y., 1949, p. 622.
- (5) Müller, E. (ed.) (Houben Weyl), 1952-.

- (6) *Reactions of SO<sub>3</sub>* (Technical Bull. SF-2), General Chemical Div., Allied Chemical & Dye Corporation, 1948.
- (7) Sidgwick, N. V., *The Chemical Elements and Their Compounds*, Vol. II, pp. 900-903, Clarendon Press, Oxford Univ., 1950.
- (8) *Sulfan* (Technical Service Bull. SF-1R), General Chemical Div., Allied Chemical & Dye Corp.
- (9) Thorne, P. C. L., and Roberts, E. R. (eds.), *Inorganic Chemistry (Ephraim)*, 5th ed., Gurney and Jackson, London, 1948.
- (10) U.S. Pat. 2,240,935 (May 6, 1941), Maurice Lepin, (to Société Rhodiaceta).
- (11) U.S. Pat. 2,403,459 (July 9, 1946), C. L. Rollinson (to Du Pont).
- (12) U.S. Pat. 2,458,718 (Jan. 11, 1949), H. G. McCann (to Allied Chemical & Dye Corp.).
- (13) U.S. Pat. 2,492,706 (Dec. 27, 1949), H. G. McCann and R. V. Townend (to Allied Chemical & Dye Corp.).
- (14) U.S. Pat. 2,511,072 (June 13, 1950), H. G. McCann (to Allied Chemical & Dye Corp.).

GREGORY FLINT

## SULFURIC AND SULFUROUS ESTERS

The esters of sulfuric and sulfurous acids, particularly the former, are familiar agents employed in organic chemistry. Since both of these acids are dibasic, a variety of esters is possible and known. Both hydrogens may be replaced by the same or dissimilar aliphatic groups, one hydrogen may be retained, or cyclic derivatives in which both hydrogens are replaced by one organic group are possible. Further, the related alkyl acid halides in which one hydroxyl group is replaced by a halogen atom are well known. The following structures illustrate the variety of compounds available:



For a discussion of the fatty alcohol sulfates, see *Sulfonation and sulfation; Surface-active agents*.

## Physical and Chemical Properties

## PHYSICAL PROPERTIES

The alkyl hydrogen esters of sulfuric acid have been reported to be oily, low-melting liquids, soluble in ether. The presence of enough water to form the monohydrate apparently causes insolubility in such solvents (12). Conductivity measurements upon aqueous solutions show that methyl hydrogen sulfate is as completely ionized as hydrochloric acid. Salts of the esters may be prepared by addition to the reaction

mixture of hydroxides or carbonates of metals whose sulfates are water-insoluble. Addition of a metal sulfate allows the desired soluble salt of the alkyl hydrogen sulfate to be separated from the insoluble metal sulfate.

The alkyl sulfates, with the exception of the cyclic derivatives, generally are liquids with rather pleasant odors. However, *n*-nonyl and the higher normal aliphatic sulfates are solids. See Table I. Their stability toward storage under normal conditions is usually quite good. The dicyclic glyoxal sulfate has a reputation for short shelf-life, although it is much more stable if all traces of the sulfuric acid used in its preparation are removed. The sulfates dissolve readily in the common organic solvents and, for the most part, can be considered water-insoluble.

The alkyl sulfites have been studied far less than the sulfates. Most of those reported are liquids of slightly lower boiling points than the corresponding sulfates. See Table II.

A large number of alkyl halosulfonates and halosulfinates are known. The lower members are high-boiling liquids: methyl chlorosulfonate,  $b_{60}$  35°C.; ethyl chlorosulfonate,  $b_{117}$  72°C. The alkyl halosulfonates appear to be much more stable to storage and moisture than the halosulfinates. Methyl fluosulfonate,  $b_{15}$  92°C., is said to corrode glass.

#### REACTIONS

*Pyrolysis* of alkyl hydrogen sulfates, with the exception of the methyl ester, yields unsaturated hydrocarbons. At 130–140°C. the methyl ester is converted to dimethyl sulfate and sulfuric acid. At lower temperatures, the reverse reaction is observed, dimethyl sulfate and sulfuric acid yielding methyl hydrogen sulfate (12).

Commercially, the most important reaction of alkyl hydrogen sulfates is *hydrolysis* to alcohols, particularly ethyl alcohol, isopropyl alcohol, and *sec*-butyl alcohol (see *Alcohol, industrial*; *Butyl alcohols*; *Propyl alcohols*).

Otherwise, the sulfuric and sulfurous esters are best known as *alkylating agents*, particularly of phenols and amines. Alkyl chlorosulfonates, sulfates, and sulfites have been most widely used in this manner. The reaction is usually performed in alkaline solution or suspension or upon the alkali salts of the phenols.

From an industrial viewpoint, only diethyl and dimethyl sulfate are of real importance.

TABLE I. Alkyl Sulfates.

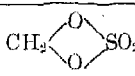
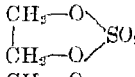
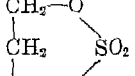
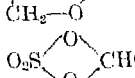
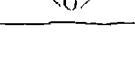
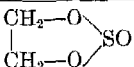
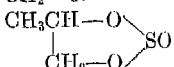
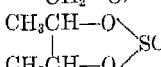
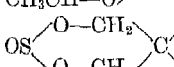
Compound	B.p., °C./mm.	Compound	M.p., °C.
$(\text{CH}_3\text{O})_2\text{SO}_2$	69–70/10		155
$\text{CH}_3\text{OSO}_2\text{OC}_2\text{H}_5$	85/15		
$(\text{C}_2\text{H}_5\text{O})_2\text{SO}_2$	89/9		99
$\text{C}_2\text{H}_5\text{OSO}_2\text{OCH}_2\text{CH}_2\text{CH}_3$	107/18		
$(\text{CH}_3\text{CH}_2\text{CH}_2\text{O})_2\text{SO}_2$	95/5		63
$[(\text{CH}_3)_2\text{CHO}]_2\text{SO}_2$	80/4		
$(\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{O})_2\text{SO}_2$	97/3		
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OSO}_2\text{OC}_2\text{H}_5$	117/20		
$\text{ClCH}_2\text{OSO}_2\text{OCH}_3$	92/18		
$(\text{ClCH}_2\text{O})_2\text{SO}_2$	97/14		
$(\text{ClCH}_2\text{CH}_2\text{O})_2\text{SO}_2$	150/7		176

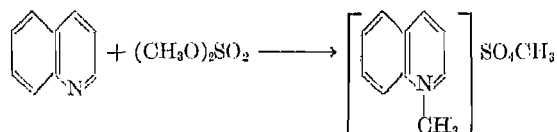
TABLE II. Alkyl Sulfites.

Compound	B.p., °C./mm.	Compound	B.p., °C./mm.
(CH <sub>3</sub> O) <sub>2</sub> SO	126-7		80/28
CH <sub>3</sub> OSOOC <sub>2</sub> H <sub>5</sub>	140-2		84/28
(C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> SO	159-60		72/12
(CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> SO	89/15		154 <sup>a</sup>
[(CH <sub>3</sub> ) <sub>2</sub> CHO] <sub>2</sub> SO	78/20		
CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> OSOCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>	104/15		
(CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> SO	110/15		
[(CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> CHO] <sub>2</sub> SO	149/1.5		
(CICH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> SO	148/45		

<sup>a</sup> Melting point.

Dimethyl sulfate reacts with phenol slowly at 110-120°C. with formation of much by-product. In aqueous alkaline solution, at about 30°C., the first methyl group reacts. At 100°C. the second methyl group is used, a 95% yield of anisole being obtained. With diethyl sulfate, higher temperatures are generally necessary; 50-55°C. is necessary to remove the first ethyl group, and the second ethyl group is utilized only at about 145°C. Alkylation of phenol in the presence of potassium carbonate in aromatic hydrocarbons is not successful, although the halogenated and nitrated phenols, which are more acidic, do react. Thiophenols are also easily alkylated by means of alkyl sulfates.

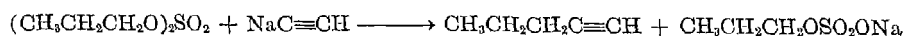
Amines, such as aniline or aliphatic amines, are readily alkylated, one of the alkyl groups of the sulfate being utilized. Tertiary amines and aromatic nitrogen heterocycles when heated with alkyl sulfates form quaternary compounds. For example, quinoline and dimethyl sulfate give methyl 1-methylquinolinium sulfate:



Aromatic hydrocarbons, such as benzene or biphenyl, which normally undergo Friedel-Crafts alkylation with other alkylating agents, react well with the alkyl sulfates in the presence of aluminum chloride. Usually, good yields of the expected alkylated hydrocarbons are realized. The longer-chain esters, such as di-*n*-butyl sulfate, behave like the halides, and a mixture of isomeric alkylated hydrocarbons results.

The alkali salts of inorganic acids when treated with alkyl sulfates yield the expected products. For instance, dimethyl sulfate and sodium iodide give methyl iodide in excellent yields; distillation of diethyl sulfate with dry potassium cyanate is perhaps the easiest laboratory method of obtaining ethyl isocyanate, and the reaction of *n*-butyl hydrogen sulfate with sodium sulfide gives mixtures of *n*-butyl mercaptans and sulfides.

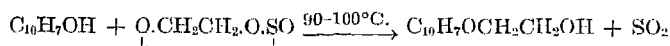
Sodium acetylide when treated with alkyl sulfates gives the corresponding alkyl acetylide. For example:



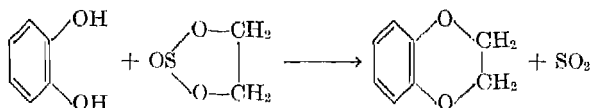
Enolic salts, such as the sodium derivative of ethyl malonate, may be alkylated by means of alkyl sulfates, which react much like alkyl halides.

The literature concerning the alkyl sulfites is not as extensive as that of the sulfates, but similar reactions are reported (3,12). Phenols and amines are alkylated by the sulfites in excellent yields, much as in the case of the sulfates. Quaternary salts of corresponding types are obtained with ease.

Ethylene sulfite, which has recently been offered in pilot-plant quantities, in many instances can replace the troublesome ethylene oxide as a means of replacing the hydrogen of phenolic or amino groups with the 2-hydroxyethyl group. Pressure equipment, usually needed with ethylene oxide, is not necessary with the sulfite. Thus with 2-naphthol:



Two *o*-hydroxy groups can react to give a cyclic compound:



### Preparation

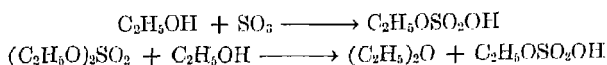
The **alkyl hydrogen sulfates** (alkylsulfuric acids) are generally prepared by the action of a sulfating agent such as sulfuric acid or sulfur trioxide upon the corresponding alcohol or by the addition of sulfuric acid to an unsaturated hydrocarbon (12). With the exception of ethylene, the olefins give esters of branched-chain alcohols. Other agents, such as dry sodium bisulfate, sulfuryl chloride, and particularly chlorosulfonic acid, are also useful. The action of an excess of 100% sulfuric acid upon normal primary alcohols gives excellent yields of alkyl hydrogen sulfates, whereas branched primary, secondary, and tertiary alcohols give less satisfactory results because of side reactions such as dehydration and ether formation.

*Methyl hydrogen sulfate* may be prepared in yields of 98–99% by treating sulfur trioxide with methanol below 0°C. (4). Sulfuric acid and methanol below 100°C. give excellent yields of the ester, although an excess of the alcohol promotes formation of methyl ether.

The preparations of *ethyl hydrogen sulfate* and its salts by the reaction of sulfuric acid and ethyl alcohol and the absorption of ethylene by sulfuric acid were among the earliest organic reactions studied. The literature on these reactions is voluminous and contradictory, although the equilibrium and reaction-velocity values seem to have been rather well established (12).

Because of the commercial importance of alcohol from this source, the reaction of ethylene and sulfuric acid has been thoroughly investigated. (See also Vol. 1, p. 278.) Ethylene in natural gases and in cracked petroleum fractions has been utilized for this purpose. Optimum conversions appear to be realized with 93–96% sulfuric acid at 60–75°C. and with good agitation to increase contact area. The presence of ethyl hydrogen sulfate seems to have an autocatalytic effect upon the rate of reaction, perhaps because of increased ethylene solubility.

In the laboratory, or for commercial batch runs, probably the more reliable reactions are those between sulfur trioxide and ethyl alcohol or between diethyl sulfate and ethyl alcohol followed by vacuum distillation of the ether formed.

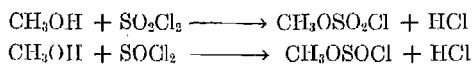


Propylene and butylene are much more readily absorbed by sulfuric acid than ethylene, and acid of lower concentration can be employed advantageously. Actually, in order to avoid side reactions, concentrated sulfuric acid should not be used, and the use of an inert solvent or a relatively slight pressure is recommended to eliminate polymerization. For example, isopropyl hydrogen sulfate may be prepared in high yield by absorption of propylene in 65–80% sulfuric acid at 10–30°C. at pressures above 50 p.s.i.

Substituted alkyl hydrogen sulfates are also readily prepared. For example, 2-chloroethyl hydrogen sulfate is readily prepared by treating ethylene chlorohydrin with sulfuric or sulfamic acid. Heating 2-hydroxyethylammonium hydrogen sulfate (ethanolamine sulfate) above 130°C. leads to the formation of 2-aminoethyl hydrogen sulfate.

The alkyl hydrogen sulfites are quite unstable and very little is known of their reactions or properties.

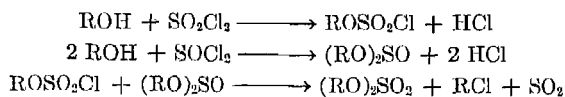
A general method of preparation of the **alkyl halogen sulfonates and sulfinates**, useful in synthesis, is the treatment of the alcohol with sulfuryl or thionyl chloride at low temperatures, meanwhile passing an inert gas through the mixture to remove hydrogen chloride (5,6,7,8,12,13):



Fluosulfonic acid and chlorosulfonic acid react with ethyl alcohol to give good yields of ethyl fluosulfonate and ethyl chlorosulfonate. Ethylene reacts exothermally with a mixture of sulfuric and chlorosulfonic acids to give ethyl chlorosulfonate in excellent yields.

The most familiar alkyl esters of sulfuric and sulfurous acids are those in which both hydrogens are replaced by organic groups.

**Alkyl sulfates** have figured much more prominently in organic chemistry, particularly in industry, than the sulfites. A general method for their preparation is given by the following scheme:



For the mixed esters, perhaps the following process is most readily adapted for laboratory use:



The only two sulfates (other than the fatty alcohol sulfates) that have achieved commercial importance are dimethyl sulfate and diethyl sulfate. A variety of methods for their manufacture have been proposed.

*Dimethyl sulfate* was prepared in Germany by a simple process employing sulfur trioxide and methyl ether (2). These two reactants were metered into columns filled with dimethyl sulfate at a carefully controlled temperature of 40°C. The dimethyl sulfate formed overflowed through an apparatus designed to test the specific gravity of the product. At consumption rates of 14.5 kg. and 25 kg./hr. of methyl ether and sulfur trioxide, respectively, an output of 39 kg./hr. of crude ester was realized. The

product was slurried with anhydrous sodium sulfate and distilled *in vacuo*. All equipment used in the process was fabricated of aluminum. A crude charge of 2250 kg. to the still gave 2200 kg. of dimethyl sulfate of 99.3% purity. The 1943 production of this plant was 1,371,000 kg., or slightly over 1500 tons.

Dimethyl sulfate may be packed and shipped in a variety of containers from glass bottles of 1-lb. capacity to tank cars. The material is classed as a corrosive liquid and rigid I.C.C. regulations, no exemptions, must be observed. All containers must bear the I.C.C. specification labels.

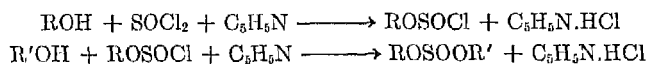
*Diethyl sulfate* has been prepared by a wide variety of methods, including the reactions of ethyl alcohol with sulfur trioxide or sulfuric acid and the vacuum distillation of ethyl hydrogen sulfate. If the demand for diethyl sulfate were great enough, the addition of sulfuric acid to ethylene, in view of the latter's widespread occurrence, would no doubt make it the cheapest available ester of sulfuric acid. The use of pressures greater than atmospheric permit the efficient use of gases containing relatively small amounts of ethylene.

In August, 1954, the price of dimethyl sulfate was 15¢/lb. and that of diethyl sulfate was 19¢/lb.

Sulfuric acid absorbs propylene much more readily than ethylene. Excellent yields of *isopropyl sulfate* are obtained by the reaction of propylene and 98% sulfuric acid at low temperatures.

A few *cyclic sulfates* are worthy of mention. Methylene sulfate is obtained by the action of sulfuric or chlorosulfonic acid on trioxymethylene (*s*-trioxane). Glyoxal sulfate 1,1,2,2-ethanetetrol bis(cyclic sulfate) (see p. 506), has been prepared commercially by the reaction of oleum (65%) and 1,1,2,2-tetrachloroethane in the presence of mercury catalysts (1).

The most successful method of preparing either symmetrical or mixed **sulfites** is the stepwise reaction of thionyl chloride with either two moles of an alcohol or molar equivalents of two alcohols in pyridine (5,6,7,8,13):



Cyclic sulfites have been prepared by this method and, in a number of cases, good yields have been realized without the use of pyridine. For example, a 90% yield of ethylene sulfite was obtained by merely allowing equimolar amounts of ethylene glycol and thionyl chloride to react at 40–50°C. Another facile reaction is the formation of the polycyclic pentaerythritol disulfite (see p. 506) from pentaerythritol and sulfur monochloride or thionyl chloride (9).

### Health and Safety Factors

The alkyl sulfates are generally liquids which constitute only moderate fire hazards.

However, dimethyl sulfate, the best-known of these esters, is an exceedingly dangerous poison (11). The maximum allowable concentration of its vapors in air is 1 p.p.m. Exposure to 97 p.p.m. for 10 min. can be fatal. The vapors cause severe inflammation of the eyes, mouth, and respiratory system. Ingestion causes convulsions and paralysis, with later damage to the kidneys, liver, and heart. Contact with the skin, through which it can be absorbed, causes severe blistering.

The fact that the symptoms of dimethyl sulfate poisoning are often delayed permits unnoticed exposure to lethal doses. There is no record of chronic poisoning.

In view of the foregoing, the precautions to be observed in handling these materials, especially dimethyl sulfate, are obvious. Impermeable gloves should be worn when opening the containers or transferring the esters from vessel to vessel, and these operations should always be performed in a hood or with other good ventilation. Only mechanical pipetting of such materials should be permitted. If the liquid should come in contact with the skin, the exposed areas should be flushed immediately with copious quantities of water, then soaped and rinsed thoroughly. The low vapor pressure of dimethyl sulfate is a factor which allows its use under conditions which would otherwise be impractical.

### Uses

The uses of the several types of esters of sulfuric and sulfurous acid have ranged from solvents to pesticides. Undoubtedly, however, chemical reactions such as alkylation or use as intermediates in the preparation of products such as ethyl alcohol have consumed the largest tonnage.

According to captured German documents, methyl hydrogen sulfate was used as a solvent in the bromination of indigoid dyes on a large scale (4). The alkyl hydrogen sulfates have also served as intermediates in the commercial preparation of various alcohols from unsaturated hydrocarbons.

The continued action of sulfur trioxide at 50–55°C. upon ethyl hydrogen sulfate (prepared from ethyl alcohol and sulfur trioxide) has been employed commercially to prepare a  $\beta$ -sulfonic acid as an intermediate in the manufacture of 2-hydroxyethane-sulfonic acid (isethionic acid),  $\text{HOCH}_2\text{CH}_2\text{SO}_3\text{H}$ .

2-Aminoethyl hydrogen sulfate has been proposed for introducing aminoalkyl groups into cotton, thereby conferring increased take-up of direct dyes as well as affinity for acid wool colors (10).

Alkyl sulfates, particularly dimethyl and diethyl sulfates, have found their largest use in alkylating phenols and amines (see *Amino phenols*; *Phenolic ethers*), which are important intermediates in the manufacture of dyes. The amine salts of ethylene glycol monosulfate have been proposed as flameproofing agents in paper manufacture (16). Dimethyl sulfate was once used as a war gas (11). Glyoxal sulfate has been used on a commercial scale in the manufacture of a few vat dyes by condensation with several polynuclear intermediates (1).

A number of alkyl sulfites, symmetrical and unsymmetrical, which may contain halogen, have been said to be effective in dilute solutions against red spider eggs and mites (14,15,17).

### Bibliography

- (1) Andrews, D. B., *et al.*, *Field Information Agency, Final Rept.*, No. 1313, Vol. II, 150 (1948).
- (2) Avery, J., *et al.*, *BIOS Final Rept.*, No. 986, 175, 227.
- (3) Carlson, W. W., and Cretcher, L. H., *J. Am. Chem. Soc.*, **69**, 1952 (1947).
- (4) Chamberlain, K. A. J., *et al.*, *BIOS Final Rept.*, No. 1482, 6 (1946).
- (5) Denivelle, L., *Compt. rend.*, **208**, 1024 (1939).
- (6) Gerrard, W., *J. Chem. Soc.*, **1939**, 99.
- (7) Levailant, R., *Compt. rend.*, **190**, 54 (1930); **192**, 1738 (1930).
- (8) Levailant, R., *Ann. chim.*, **6**, 459 (1936).



- (9) Orthnet, L., *Ber.*, **61B**, 116 (1928).
- (10) Reeves, U. A., and Guthrie, J. D., *Textile Research J.*, **23**, 522 (1953).
- (11) Sax, N. I., *Handbook of Dangerous Materials*, Reinhold, N.Y., 1951, p. 147.
- (12) Suter, C. M., *The Organic Chemistry of Sulfur*, Wiley, N.Y., 1944, ch. 1.
- (13) Voss, W., and Blanke, E., *Ann.*, **485**, 258 (1930).
- (14) Brit. Pat., 346,685 (Nov. 7, 1929), I. G. Farbenind.
- (15) U.S. Pat. 2,377,148 (May 20, 1945), I. Heichenbleickner (to American Cyanamid Co.).
- (16) U.S. Pat. 2,511,911 (June 20, 1950), W. M. Fuchs and E. Gavalin.
- (17) U.S. Pats., 2,529,493-4 (Nov. 15, 1950), W. O. Harris, *et al.* (to U.S. Rubber Co.).

JAMES M. STRALEY

**SULFUR NITRIDE**,  $S_4N_4$ . See *Explosives (high)*, Vol. **6**, p. 19; *Sulfur compounds, inorganic*.

**SULFUROUS ACID**,  $H_2SO_3$ . See "Sulfur dioxide" under *Sulfur compounds, inorganic*.

**SULFUR TRIOXIDE**,  $SO_3$ . See *Sulfuric acid*.

**SULFURYL HALIDES**,  $SO_2X_2$ . See *Sulfur compounds, inorganic*.

**SULTAMS; SULTONES**. See *Sulfur compounds, organic*.

**SUMAC**. See *Tanning materials*.

**SUNBURN PREVENTIVES; SUNTAN PREPARATIONS**. See *Cosmetics*, Vol. **4**, p. 559.

**SUNFLOWERSEED OIL**. See *Fats and fatty oils*, Vol. **6**, pp. 144, 147, 148.

**SUNN**. See *Fibers, vegetable*, Vol. **6**, pp. 468, 476.

**SUPERALLOYS** (high-temperature alloys). See *Iron alloys*, Vol. **8**, p. 51.

**SUPERFATTED SOAPS**. See *Cosmetics*, Vol. **4**, p. 551; *Shampoos*, Vol. **12**, p. 223.

**SUPEROXIDES**. See *Peroxides, inorganic*, Vol. **10**, p. 53.

**SUPERPHOSPHATE; TRIPLE SUPERPHOSPHATE**. See *Fertilizers (phosphoric acid)*, Vol. **6**, pp. 402, 419.

**SUPPOSITORIES**. See *Pharmaceuticals*, Vol. **10**, p. 242.

## SURFACE-ACTIVE AGENTS

For the purposes of this article, surface-active agents may be defined in terms of their behavior in dilute aqueous solution. Such solutions wet surfaces readily, remove dirt, penetrate porous materials, disperse solid particles, emulsify oil and grease, and produce foam when stirred or shaken. Because of these properties of their solutions, surface-active agents are often called wetting agents, detergents, penetrants, dispersing agents, emulsifying agents, and the like. But these properties are closely interrelated and no given surface-active agent possesses only one of them to the exclusion of all the rest. A compound is called a wetting agent rather than a detergent because its wetting power is greater than its detergent power. With almost every surface-active agent, one property predominates over the others and this property determines the general name of the compound and its field of application.

Two surface-active materials were well known long before the modern surface-active agents. These are soap (*q.v.*) and the sulfonated oils. In addition, certain naturally occurring substances have similar action, for example, the saponins (*q.v.*)

of plant origin and the clay bentonite. This article deals with the synthetic surface-active agents, sometimes referred to as "surfactants" or "syndets." They were first developed after World War I for the textile industry but have now spread, not only into a variety of other industries, but into the field of household detergents as well.

The **sulfonated oils** are made by treating the fatty oils with concentrated sulfuric acid or oleum, followed by neutralization with caustic alkali or ammonia. In the process, the water-insoluble fatty oil is transformed into a sulfonated oil that dissolves readily in water to give a clear, brilliant solution containing a considerable amount of unsulfonated oil. The sulfonated oils are used as dyeing assistants and lubricants in the manufacture of textiles. They are also widely used in the leather industry for the fat-liquoring of leather. See also *Sulfonation and sulfation*.

In 1913, Reychler reported the synthesis of cetylsulfonic acid (1-hexadecanesulfonic acid) and cetyltriethylammonium chloride. He studied many of their physical properties and emphasized their soaplike characteristics. To Reychler must be given the credit for having made the first synthetic surface-active agents to be recognized as such, but his papers seem to have attracted little or no attention in industry.

The Allied blockade of Germany during World War I, with the resulting shortage in fats, led to the development of detergents and other surface-active agents not made from fats. The first patent disclosing the use of a synthetic surface-active agent not derived from fats was filed in 1917 by Dr. Fritz Günther of Badische Anilin und Soda Fabrik. It covered the use in a detergent mixture of sodium diisopropylnaphthalenesulfonate. The first representative of the alkylarenesulfonates was put on the market in 1925 under the trade name of Nokal (sodium butylnaphthalenesulfonate) and is still used as a textile assistant both in Germany and in the U.S. The industrial development of the synthetic surface-active agents took place in Germany during the decade following the end of World War I, the first production being for the textile industry.

The need for greater production of textiles created a demand for fast-acting, more efficient products than soap. Soap was, and still is, used in large quantities by the textile industry but it has certain disadvantages; it forms sticky, curdlike precipitates in hard water and in acid solutions. In hard water the precipitate consists of the calcium or magnesium salts of the fatty acids used to make the soap, and in acid solutions it consists of the fatty acids themselves. These precipitates are particularly objectionable in textile finishing because they are hard to wash out of the goods completely and if they remain during the dyeing operation may cause light spots to show up on the finished fabric. In addition, the use of soap in hard water results in a considerable economic loss to the textile industry, since soap is used up in reacting with the calcium and other ions.

In the first attempts to make detergents having the good characteristics of soap but with greater resistance to hard water and acids, the soap molecule was used as the pattern for the new products. It had long been known that the sensitivity of soap to hard water and acids was due to the presence of the carboxyl group. Accordingly, means were sought to replace or modify the carboxyl group while still retaining the general configuration of the soap molecule that is responsible for its surface-active properties.

One way was to replace the carboxyl group by an hydroxyl group and then, by treatment of the latter with sulfuric acid or oleum, to produce a sulfated fatty alcohol (alcohol prepared by reduction of one of the fatty acids, *q.v.*). In this way, the long hydrocarbon chain of the fatty acid remained intact and a solubilizing group far more resistant to hard water and acids was introduced. However, with the exception of cetyl alcohol (1-hexadecanol), a constituent of spermaceti, there were no fatty alcohols then commercially available. The first problem was to produce fatty alcohols in quantity.

The only method known at the time for doing this was a laboratory procedure, the Bouveault-Blanc reaction. It consists of reducing the esters of fatty acids with metallic sodium in alcohol. But at that time it hardly seemed possible to adapt this procedure to a manufacturing scale, so workers in the field looked for other methods. The high-pressure catalytic hydrogenation of fatty esters and even of the fatty acids themselves was worked out by several different groups of chemists simultaneously. This has been the chief method for making fatty alcohols, although the sodium reduction method is now also used on a commercial scale.

The conversion of fatty acids into fatty alcohol sulfates was not the only means used to overcome the disadvantages of the carboxyl group. Another method was to block this group by convert-

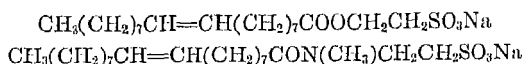


TABLE I. Selected Commercial Surface-Active Agents (Concluded).

Brand Name	Manufacturer	Chemical Name, Formula, or Description	Class	Main Uses
Ethyl Cetab	Fair.	Cetyltrimethylethylammonium bromide	C	G
Hyamine 1622	R&H	$(p\text{-C}_6\text{H}_4\text{C}_6\text{H}_4\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{X})(\text{CH}_3)_2(\text{C}_6\text{H}_4\text{CH}_2)\text{NCl}$ ( $\text{C}_6\text{H}_4\text{X}$ — is "diisobutyl," $(\text{CH}_3)_2\text{CCH}_2\text{C}(\text{CH}_3)_2\text{—}$ )	C	G
Igepal CA	Antara	$\text{RC}_6\text{H}_4\text{O}(\text{CH}_2\text{CH}_2\text{O})_n\text{H}$ ; (R = alkyl)	N	W, Det, E
Igepon T	Antara	Sodium <i>N</i> -methyl- <i>N</i> -oleylaurate	A	Det, W
Igepon A	Antara	Sodium oleylisethionate	A	Det, W
Intramine	Synth.	$\text{RCONHCH}_2\text{CH}_2\text{OSO}_3\text{Na}$ (R $\text{COOH}$ = commercial lauric acid containing myristic acid)	A	W, E
Invadine C	Giba	Sodium alkylnaphthalenesulfonate	A	W
Leonil SA	Antara	Sodium dibutylnaphthalenesulfonate	A	W
Marasperse C	Mara.	Highly purified sodium lignin sulfonate	A	Dis
Maypon 4C	Maywood	Condensation product from protein and oleyl chloride	A	Det, W, E
Miranols	Miranol	$\text{C}_{11}\text{H}_{23}\text{C} \begin{array}{c} \text{N}-\text{CH}_2 \\ \text{N}-\text{CH}_2 \end{array} \begin{array}{c} \text{N}-\text{CH}_2 \\ \text{N}-\text{CH}_2 \end{array} \text{OH} \begin{array}{c} \text{CH}_2\text{CH}_2\text{ONa} \\ \text{CH}_2\text{COONa} \end{array}$	A	Det
Myrj 45	Atlas	Polyethylene glycol stearate	N	E
Nacconol NR	Natl. An.	Sodium "dodecyl"benzenesulfonate	A	Det, W
Nekal A	Antara	Isopropylated naphthalenesulfonic acid (Na salt)	A	W
Nekal BX	Antara	Butylated naphthalenesulfonic acid (Na salt)	A	W
Ninol 1281	Ninol	Fatty acid alkanolamide, as $\text{RCONHCH}_2\text{CH}_2\text{OH}$	N	Det
Nonic 218	Sh.	$\text{C}_{12}\text{H}_{25}\text{S}(\text{CH}_2\text{CH}_2\text{O})_n\text{CH}_2\text{CH}_2\text{OH}$ ( $\text{C}_{12}\text{H}_{25}$ = "tert-dodecyl" from polymerized isobutylene)	N	Det, W
Plurionics	Wy.	Condensation product of ethylene oxide and polypropylene glycol	N	Det, E, Dis
Renex 25	Atlas	Solidified urea complex of polyethylene glycol ester of mixed fatty and resin acids	N	Det
Roccal	Win.	Alkylbenzyltrimethylammonium chloride	C	G
Santomerse No. 1	Mons.	Sodium "dodecyl"benzenesulfonate	A	Det
Santomerse D	Mons.	Sodium decyl benzenesulfonate	A	Det, W
Santomerse B	Mons.	$m\text{-C}_6\text{H}_4\text{COOC}_{12}\text{H}_{25}(\text{SO}_3\text{Na})$	A	Det
Sapamine KW	Giba	$[\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{CONHCH}_2\text{CH}_2\text{N}(\text{CH}_3)(\text{C}_2\text{H}_5)_2] + [\text{CH}_3\text{OSO}_3]^-$	C	W
Span 40	Atlas	Sorbitan monopalmitate	N	E
Span 80	Atlas	Sorbitan monooleate	N	E



ing it into an ester or an amide. The free carboxyl group was tied up and at the same time a more strongly acidic group, far less sensitive to hard water, was introduced. The first compounds made in this way are known as Igepon A and Igepon T and have the following structures, respectively:



The alkylarenesulfonates, the fatty alcohol sulfates, and the blocked fatty acid derivatives, as well as others to be described later, were well established in the textile industry by the early 1930's and since that time there has been tremendous activity in the field. J. W. McCutcheon (21,58,59) has given a list of almost one thousand commercially available products.

Although the industrial applications of surface-active agents have grown tremendously, household cleaners consume the greatest volume of these materials today. This amounts to about one billion pounds a year and is probably twice as much as that consumed for all industrial purposes. However, the number of different surface-active compounds used in household cleaners is quite small in comparison with the number used for industrial purposes.

A selected list of commercial surface active agents is given in Table I. A very extensive list is given in (21) and (58). See also (59). It should be emphasized that the last column of Table I is selective; often a given surface-active agent has other uses besides those given here.

### Classification

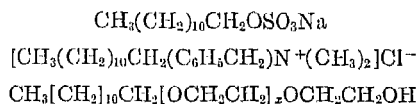
Surface-active agents are divided into two broad classes according to the character of their colloidal solutions in water. Compounds belonging to the first class, the **ionic** surface-active agents, form ions in solution and like the soaps are typical colloidal electrolytes. Compounds of the second class, known as the **nonionics**, do not ionize but owe their solubility to the combined effect of a number of weak solubilizing groups such as ether linkages or hydroxyl groups in their molecules.

The general properties and behavior of surface-active agents are due to the dual character of the molecules of these substances. Their molecules are made up of two parts, a relatively large, elongated part, the hydrophobic group, and a small solubilizing, polar group, the hydrophilic group. The antagonism of these two portions of the molecule and the balance between them gives the compound its surface-active properties. The hydrophilic group exerts a solubilizing effect and tends to draw the entire molecule into solution; the hydrophobic group, on the other hand, because of its insolubility, has the effect of resisting this tendency. If the proper balance between the two groups exists the substance neither dissolves completely nor remains completely undissolved but concentrates at a liquid-liquid interface, its molecules so oriented that the hydrophilic groups are anchored in the aqueous phase and the hydrophobic groups project into the nonaqueous phase.

The proper balance between the two kinds of groups is important and may be illustrated by reference to the sodium salts of the aliphatic acids. In the lower members of the series, such as sodium acetate and sodium propionate, the effect of the hydrophilic group so far outweighs the weakly hydrophobic properties of the short hydrocarbon chain that the compound dissolves completely. At the other end of the scale the sodium salts of carboxylic acids of twenty carbons or more are practically insoluble. Those in the intermediate range, ten to eighteen carbon atoms, make up the soaps.

The ionic class is further subdivided in accordance with the way its members behave upon ionization. If, upon ionization, the ion containing the large hydrophobic

group assumes a negative charge and becomes the anion, the compound is classified as an *anionic* surface-active agent. In this case the cation will consist of a simple metallic ion such as sodium or potassium ion. If, on the other hand, the reverse is true and the ion containing the hydrophobic group takes on a positive charge and becomes the cation, the compound is classed as cation active or *cationic* surface-active agent. In this case the anion will usually consist of chloride or bromide ion. Thus there are three major classes, the anionic, the cationic, and the nonionic surface-active agents. A typical example of each of the three classes of surface-active agents is shown:



The great majority of surface-active agents belong to the anionic class. In 1952 this class comprised about 85% of all the surface-active agents made in the U.S. The cationics, on the other hand, are less important as surface-active agents but are important for another reason. One group, the surface-active quaternary ammonium salts (*q.v.*), were found to possess extremely high bactericidal power. They are therefore produced in large quantities for use as disinfectants in medicine and sanitation. Nonionic surface-active agents, although still a small class compared to the anionics, are growing rapidly and are replacing them for many uses. They are not only excellent wetting agents, detergents, emulsifiers, etc., but also have the advantage of being compatible with many substances that react with and inactivate the anionics and the cationics.

### Physical Properties

Pure surface-active compounds have been very little studied. Attention has rather been focused on the commercial surface-active agents which consist of mixtures and which cannot be characterized by definite physical properties. For example, the fatty alcohol sulfates of commerce are made from alcohols obtained by reducing fats containing mixtures of fatty acids. These mixed alcohols are sometimes distilled to concentrate those in the twelve and fourteen carbon range. Nevertheless, the product always contains alcohols of several different chain lengths. In the manufacture of typical alkylarenesulfonates such as *dodecylbenzenesulfonate* (see p. 523) the petroleum fraction used to form the side chain is so chosen as to have an average molecular weight corresponding to twelve carbon atoms but is, of course, a mixture. For the most part, the cationics and nonionics are also mixtures. Amines derived from the mixed fatty acids of coconut oil are used in some of the most widely known cationic products on the market. Mixed fatty acids or alcohols are used as starting materials for the preparation of many nonionics.

Surface-active agents, when free from inorganic salts, are generally pasty or gelatinous materials resembling the soaps in consistency and are difficult to purify by crystallization. However, they usually contain sodium sulfate, derived from an excess of sulfuric acid which is generally used in preparation of the anionic surface-active agents, and which is ordinarily not removed. In fact, more sodium sulfate is sometimes added so as to produce a mixture containing about 35–40% of active ingredient and 60–65% sodium sulfate. The presence of sodium sulfate has several advantages.

It provides a product which is readily dried to a free-flowing flake or bead, depending upon the method used. Also, the active ingredient is supplied in a concentration convenient for use, since in many applications of surface-active agents concentrations as low as 0.1 to 0.2% are common. Furthermore, the sodium sulfate acts to some extent as a builder for the surface-active agent. (See also *Detergency*.) The cationic surface agents that find application chiefly as germicides and sanitizing materials are used in such dilutions that they are often sold in water solutions which may be further diluted for use. To some extent the same is true for the nonionic compounds, although many are often sold in paste form. Recently processes have been developed for producing nonionic surface-active agents in dry powder form by mixing them with certain other materials suitable for the purpose.

There is voluminous literature on the physical chemistry of solutions of surface-active agents. Most of the fundamental work has been done on soaps, since the synthetic surface-active agents are relatively new. McBain pioneered in the colloid chemistry of soaps and surface-active compounds, and his work has been of major importance in the field. In fact, he was responsible for the basic concept of colloidal electrolytes, the class of substances to which soaps and surface-active agents belong. See also *Colloids*; *Surface properties*.

It is the common practice to speak of such phenomena as detergency, wetting, foaming, dispersion, and emulsification as properties of surface-active compounds. Schwartz and Perry (30) have very aptly called them gross effects of surface-active agents rather than properties. It should be pointed out that these properties are quite complex and are made up of a number of factors that are quite difficult to measure and each one of which contributes to the gross effect. Thus, a complex effect such as detergency cannot be estimated by determining one easily measurable physical property of a solution, lowering of surface tension, for example. Although there is, of course, a relationship between detergency and surface tension lowering, the fact that any given compound lowers the surface tension of water to half or less of its normal value is no indication that the compound will have any detergent properties. However, as Fischer and Gaus have indicated (8), it may be possible in the future, by the careful measurement of a number of properties of surface-active solutions, such as contact angle, lowering of surface tension, interfacial tension, and others, to establish correlations between such measurements, which will serve as a basis for estimating the more complex phenomena of wetting, detergency, and emulsification.

### Effect of Structure on Properties

In any given surface-active compound, the hydrophobic group is relatively large and, in the majority of cases, consists of a paraffin chain or an aromatic ring to which a paraffin chain is attached. In the case of the anionic compounds, the hydrophilic group, with few exceptions, is either  $-\text{OSO}_3\text{Na}$  or  $-\text{SO}_3\text{Na}$ . The reason for this is that, whereas other mineral acids may be and sometimes are used, sulfuric acid is not only the cheapest acid but the easiest to introduce into an organic molecule. The hydrophilic group of the cationic compounds consists almost without exception of tetravalent nitrogen in the form of a quaternary ammonium salt. The hydrophobic groups in the nonionic compounds are the same as those in the other two classes of surface-active agents, but the hydrophilic groups are quite different. They are generally end-substituted polyethylene glycols,  $\text{R}(\text{OCH}_2\text{CH}_2)_n\text{OH}$ , where R is the hydro-



phobic group and the hydrophilic group is a chain of ethylene oxide units (ethoxy groups) ending in a hydroxyl group. The properties of the nonionics may be widely varied by varying the length of the hydrophilic chain. Other groups containing several hydroxyls serve as hydrophilic groups in certain nonionics.

There is a definite relationship between the chemical constitution of surface-active agents and their surface-active behavior. This is apparent from the fact that anionic, cationic, and nonionic surface-active agents act quite differently in solution. In addition, compounds of different structures behave differently within each of the three classes. For example, long-chain alcohol sulfates in which the hydrophilic group is at the end of the chain are among the best detergents known, although they have only average wetting power, while those in which the hydrophilic group is near the middle of the chain have little or no detergent action but are among the most powerful wetting agents available (7).

A number of other cases are known in which a relatively small change in the structure of a surface-active compound produces a profound change in its surface-active behavior. However, up to the present time, little systematic work has been done on the relationship between the chemical constitution of surface-active compounds and their performance. A great deal more painstaking work will be needed before structure can be correlated with performance in any but isolated cases (25). Such correlation can only be based upon the synthesis of a large number of surface-active compounds in which the structures are systematically varied. The structure and the purity of the compounds must be definitely established and their surface-active properties studied by means of carefully standardized tests. One of the very few studies to be found in the literature that meets the required conditions is that of Dreger, Shedlovsky, *et al.* (7). These investigators prepared several series of purified sodium salts of long-chain alcohols in which chain length and position of the hydrophilic group were varied. The effect of these changes in structure upon such properties as detergency, wetting, foaming, and surface tension lowering were then measured. Neville and Jeanson (23) studied the relation between structure and surface tension lowering in a series of sodium mono- and dialkylbenzenesulfonates and found that two substituents were more effective than one. They also found that sodium *o*- and *p*-toluenesulfonates differed in their ability to depress surface tension, the ortho isomer being more effective.

Gotte (9) studied the detergent power of a homologous series of pure fatty alcohol sulfates (even number of carbon atoms) and at 60°C. found it to lie in the order  $C_{16} > C_{14} > C_{18} > C_{12}$ . He also studied the foaming power of the same compounds and the way in which this was affected by temperature. Venkataraman and his co-workers (38) prepared a series of fatty acid amides of aromatic amino sulfonic acids and studied the wetting power and certain other properties of the compounds. The structures were varied so as to observe the effect of such factors as the position of the hydrophilic group, unsaturation in the carbon chain of the fatty acid, molecular weight, and the presence of halogen and methyl groups.

### Anionic Agents

#### ALKYLARENESULFONATES

The alkylarenesulfonates, commonly called alkyl aryl sulfonates, were the first synthetic surface-active agents to be developed, and they are produced in larger

quantities today than any other type. Until World War I, all the surface-active agents known were based upon compounds containing straight aliphatic carbon chains. It was quite surprising, therefore, to discover that an aromatic sulfonate with two short side chains possessed surface-active properties, and this led to tremendous activity in this field of compounds. Almost every conceivable type of alkylated aromatic hydrocarbon has been prepared, sulfonated, and tried out as a surface-active agent. Alkylarenesulfonates derived from benzene, naphthalene, diphenyl, diphenylmethane, and many other compounds have been described in the patent literature. The most widely used are benzene and naphthalene because of their low cost and ready availability. The volume of surface-active agents derived from these two hydrocarbons alone far exceeds that of any other class. In 1952 it amounted to more than 40% of all the surface-active agents produced.

Even though certain other classes of compounds have superior surface-active properties, the alkylarenesulfonates are more widely used because they are potentially the cheapest to manufacture and have other advantages. One advantage is that their properties may be widely varied by easily made changes in their structures. Different aromatic nuclei may be chosen as starting materials, and the number, position, and length of the side chains attached to them may be varied. More than one sulfonate group may also be introduced, but in most cases this makes the compound too soluble and reduces its surface activity. Another advantage of the alkylarenesulfonates is their great stability toward hydrolysis. Many of them can be refluxed for several hours with caustic soda solution without appreciable decomposition.

**Manufacture.** The preparation of the alkylarenesulfonates is carried out in three steps: alkylation of the aromatic nucleus, sulfonation of the resulting alkylated aromatic hydrocarbon, and neutralization of the sulfonation product with caustic soda. In the case of certain aromatic compounds, sulfonation may precede alkylation but, in general, this leads to the formation of a different product because the sulfonate group has a different orienting influence than that of alkyl groups. This procedure offers little advantage in the case of benzene since benzenesulfonic acid is quite difficult to alkylate. In certain instances when sulfuric acid is used as the alkylation catalyst, the two reactions proceed simultaneously. Caustic potash or ammonium hydroxide is sometimes used instead of caustic soda for neutralization.

Various classes of compounds may be used to alkylate aromatic nuclei for the preparation of alkylated aromatic sulfonates, the most important of which are alkyl halides, alcohols, and olefins. (See *Alkylation*.) Among the more common alkylation catalysts are aluminum chloride, sulfuric acid, and boron trifluoride. Because of the high cost of long-chain alcohols, they are relatively little used, and until recently there were no long-chain terminally unsaturated hydrocarbons available. At present, however, one of the most widely used alkylarenesulfonates is made by alkylating benzene or toluene with such a long-chain olefin. Sulfuric acid is the preferred catalyst for alcohols and olefins, whereas aluminum chloride is generally used with the alkyl halides. Isomerization occurs during the alkylation of aromatic compounds with alcohols and olefins in the presence of sulfuric acid. In the case of the normal primary alcohols, for example, the point of attachment to the aromatic nucleus is not the first, but the second, carbon atom. The olefins undergo a similar isomerization. These reactions were studied by Ipatieff, Pines, and Schmerling (13), who showed that such rearrangements did not take place when aluminum chloride was used as the catalyst.

The Friedel-Crafts reaction has long been used to alkylate aromatic hydrocarbons

for the preparation of alkylated aromatic sulfonates. Since it is known that in most cases an unbranched side chain gives the greatest surface activity in the final product, a crude petroleum in which straight paraffin chains predominate is generally selected. From this, a fraction in the kerosene range is then taken. The average molecular weight of this fraction may correspond to that of saturated hydrocarbons containing ten, twelve, or fourteen carbon atoms as desired. This hydrocarbon mixture is chlorinated by passing in chlorine at about 100°C., or at lower temperatures in the presence of certain catalysts, until the gain in weight of the mixture corresponds to approximately one mole of chlorine per mole of hydrocarbon. See also ref. (33).

The alkyl halide prepared in this way is then condensed with the aromatic compound in the presence of aluminum chloride under the experimental conditions that are usually most favorable to the Friedel-Crafts reaction. An excess of the aromatic compound is used to minimize the formation of the dialkyl derivative, the reaction temperature is kept low, and only catalytic amounts of aluminum chloride are used. When the condensation is complete, the aluminum chloride sludge is separated and the rest of the reaction mixture is subjected to distillation. If the aromatic is a low-boiling liquid such as benzene, it may be removed at atmospheric pressure and the residue then distilled under reduced pressure or used for sulfonation in the crude form. For a description of the method of sulfonation, see *Sulfonation and sulfation*.

*Dodecylbenzenesulfonate* is typical of this class of surface-active compounds. It is clear from the nature of the raw materials used to prepare them, however, that the alkylbenzenesulfonates are not pure compounds. The kerosene fraction which provides the alkyl chains consists of a mixture, and the hydrocarbons made by alkylating benzene with such kerosene fractions are often called *keryl* benzenes to indicate that, although one chain length may predominate, shorter and longer chains are also present. In addition, isomerization takes place during the Friedel-Crafts reaction, producing compounds in which the benzene nucleus is attached to a secondary rather than a primary carbon atom.

Surface-active agents of the foregoing class have excellent detergent power, and therefore are widely used as detergents in the form of mixtures with sodium sulfate containing 35–40% of active ingredient. These mixtures are used either as such or in combination with other detergent substances. They are used in several of the so-called heavy-duty household detergents which consist of spray-dried mixtures of synthetic detergents, phosphate builders, and additives to produce brightness in fabrics and to prevent redeposition of soil. Two of the oldest and best known alkylbenzenesulfonates are sold under the trade names of Nacconol NR and Santomerse. Several closely related products are marketed under the trade names of Ultrawet and Oronite.

#### SULFATED ALCOHOLS

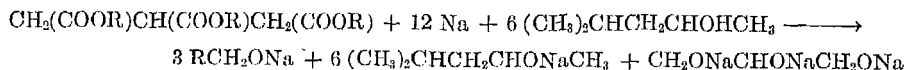
✓The most important sulfated alcohols are the fatty alcohol sulfates. They are second only to the alkylarenesulfonates in volume consumed and are generally superior to them in detergent properties. The fatty alcohol sulfates are sodium salts of the monoesters of sulfuric acid with *n*-aliphatic alcohols containing from eight to eighteen carbon atoms,  $\text{CH}_3(\text{CH}_2)_n\text{OSO}_3\text{Na}$ . They have the same general structure as soaps, but the carboxyl group has been replaced by a more strongly hydrophilic group that is far more resistant to hard water.

**Manufacture.** In contrast to the fatty acids, the *n*-aliphatic alcohols (fatty

alcohols) do not occur abundantly in nature. Only a limited number are obtainable from natural products in significant quantities. Oleyl alcohol (*cis*-9-octadecen-1-ol) is a component of the body oil of the sperm whale and certain other marine animals, and cetyl alcohol (1-hexadecanol) is a constituent of spermaceti, the waxlike solid obtained from the head of the sperm whale. Spermaceti consists of an ester, cetyl palmitate, which upon saponification with alkali yields cetyl alcohol and palmitic acid. Sodium cetyl sulfate was well known and its soaplike properties recognized, but it was necessary to have a more plentiful source of fatty alcohols before the fatty alcohol sulfates could become large-scale commercial products.

This source was provided by the development of the process for the catalytic hydrogenation of esters, glycerides, or free fatty acids at 200 atm. pressure at about 200°C. over a copper chromite catalyst. The process was worked out almost simultaneously by several groups of workers in the U.S. and in Germany in the early 1930's (2,15). The high-pressure catalytic hydrogenation process proved to be very successful and until quite recently was the only one in use for the production of fatty alcohols on a commercial scale, either as raw materials for the manufacture of detergents or for other uses. The principal alcohols used for the preparation of fatty alcohol sulfates are oleyl alcohol and the mixture of alcohols obtained by reducing coconut oil or the coconut oil fatty acids. The commercial name *lauryl alcohol* is often given to this mixture because its major component is lauryl alcohol (1-dodecanol). Coconut oil differs from the majority of fats and oils in several respects: first, it contains only saturated fatty acids, and, second, it contains a very high proportion of ten-, twelve-, and fourteen-carbon fatty acids. It is the richest source of lauric acid, which is present in it to the extent of 40–50%. The mixture of sulfated alcohols derived from coconut oil has unusual surface-active properties. It gives stable long-lasting foam and is an excellent detergent even at ordinary temperatures. Oleyl alcohol is made by reducing oleic acid or mixtures of fatty acids rich in oleic acid. (See also Vol. 1, p. 319; Vol. 6, p. 270.)

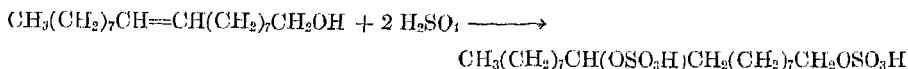
When operating under the usual conditions, the high-pressure catalytic reduction of fats and fatty acids to alcohols attacks olefinic bonds and leads to the production of saturated alcohols. Since unsaturated alcohols, particularly oleyl alcohol, are often desired, several American firms became interested in the sodium reduction process, which does not saturate the double bonds. Several full-scale plants are now in operation (14). The process is based upon the Bouveault-Blanc procedure (see p. 514). In commercial practice, the use of secondary alcohols as the reducing alcohols has proved most satisfactory. Primary alcohols react too readily with sodium, and tertiary alcohols are too slow. Obviously, the choice of the reducing alcohol will depend upon cost and availability. 4-Methyl-2-pentanol is used in at least one commercial process. A simplified equation for the reaction using this alcohol is given by Kastens and Peddicord (14):



The sodium derivatives shown in the equation are converted to the corresponding alcohols and glycerol by hydrolysis with water, and the fatty alcohol is separated from the mixture by distillation.

Concentrated sulfuric acid or oleum is generally used to convert the fatty alcohols to the sulfates, although a variety of other sulfating agents are claimed in the patent

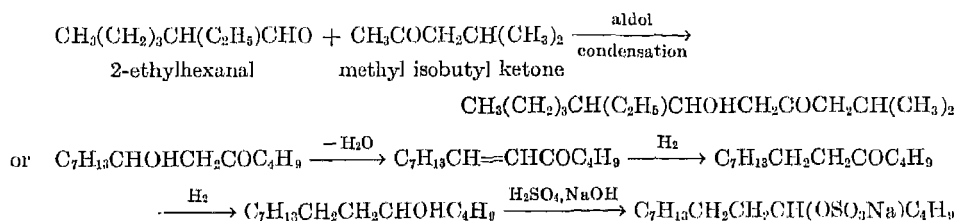
literature. The saturated alcohols present no problem since the reaction cannot be complicated by reactions at the double bond. After sulfation the reaction mass is neutralized with caustic soda. Since an excess of sulfuric acid is used, sodium sulfate is always formed along with the fatty alcohol sulfate. The sodium sulfate may be removed before drying but it is generally left in. Typical commercial fatty alcohol sulfates contain 50-60% sodium sulfate. With the unsaturated alcohols, sulfation is more complicated because the sulfuric acid not only reacts with the hydroxyl group but also adds to the double bond:



Thus, other sulfation methods must be used if it is desired to obtain fatty alcohol sulfates which contain free double bonds. This is generally the case since the surface-active properties of the unsaturated fatty alcohol sulfates are superior to those in which the double bond is sulfated. A number of methods have been reported (31) that do not involve the olefinic bonds, for example, the use of chlorosulfonic acid in the presence of an organic base such as pyridine.

The fatty alcohol sulfates that have been described are derived from primary alcohols containing even-numbered, unbranched carbon chains, since they are made from the naturally occurring fatty acids in which only such chains are present. Another important class of surface-active agents is based upon the secondary alcohols. The carbon chains in this case do not occur in nature but are built up synthetically by means of a series of chemical reactions; they are often branched and may be either odd- or even-numbered. The discovery and development of these alcohols and their sulfates are due to Wickert and his co-workers (49). Long carbon chains are built up from smaller units by use of the aldol condensation (see *Aldols*).

The following equations exemplify the steps in the preparation of one of the secondary alcohol sulfates:

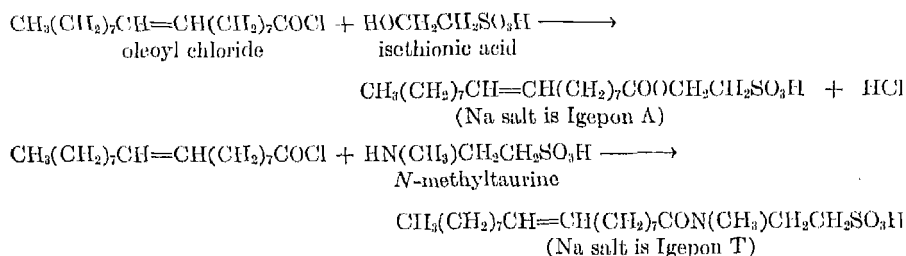


The starting materials used in the foregoing synthesis can also be made by the aldol condensation: 2-ethylhexanal by condensing two moles of butyraldehyde, and methyl isobutyl ketone by condensing acetone with itself. The secondary alcohol sulfates of the type described above are sold under the trade name of Tergitols and are among the best wetting agents on the market.

#### OTHER ANIONIC AGENTS

Compounds belonging to the two classes already described, the alkylarenesulfonates and the sulfated alcohols, make up about 90% in number of all the anionic surface-active agents produced. In bulk they are produced in greater quantities than the total of all other surface-active agents. The principal reason is that compounds of these two classes are the ones most extensively used in household detergents. The

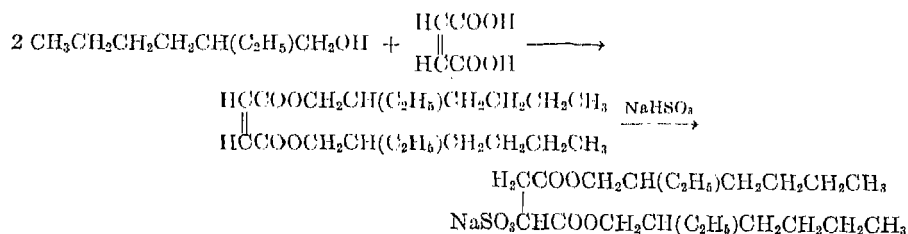
remaining 10% of the anionic surface-active agents fall into a variety of chemical classes too numerous to include in the present article. Many of them are only produced on a small scale and are restricted to specialized uses, either because of certain unusual properties or because of their relatively higher price. Accordingly, only a few of the more representative of the remaining classes of anionics will be discussed. In the preparation of the Igepons (see p. 518), the acid chloride of the fatty acid is first prepared by treating the acid with phosphorus trichloride or thionyl chloride. The fatty acid chloride is then reacted according to the following equations:



Treatment of the free sulfonic acids with caustic soda converts them into the sodium salts which are marketed under the trade names of Igepon A and Igepon T, respectively.

There are many other ways in which surface-active agents can be made by blocking the carboxyl group of fatty acids. One widely used procedure is to acylate the amino group of a low-molecular-weight hydroxy amine, such as monoethanolamine, with a fatty acid and then to sulfate the free hydroxyl group. Compounds made in this way have the general formula  $\text{CH}_3(\text{CH}_2)_n\text{CONHCH}_2\text{CH}_2\text{OSO}_3\text{Na}$ . Although the mixed fatty acids from coconut oil are most commonly used in the preparation of this class of compounds, other fatty acids may be used. The fatty acid and the monoethanolamine in equimolecular proportions are heated together in a still for several hours until the acid number of the reaction mass falls below 5. The water evolved in the reaction is allowed to escape. The reaction product is then sulfated by the addition of sulfuric acid monohydrate (100%  $\text{H}_2\text{SO}_4$ ) with stirring and cooling so as to maintain the temperature at 30 to 35°C. The products are said to be excellent foamers and detergents with good lime stability (43).

The esters of sodium sulfosuccinic acid form another important class of surface-active agents (46,54). They are prepared by esterifying maleic acid with alcohols in the four to eight carbon range and subsequently adding sodium bisulfite at the double bond of the unsaturated ester:



Many esters of sodium sulfosuccinic acid have been prepared and their properties studied (4). Several of them are well-established commercial products that are sold under the trade names Aerosol or Decerosol by American Cyanamid Co., and they are the

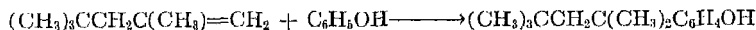
most powerful wetting agents on the market. The bis(2-ethylhexyl) ester shown in the above equations is known as Aerosol OT.

The *sodium salts of sulfated monoglycerides*, having the structure  $\text{CH}_3(\text{CH}_2)_n\text{COOCH}_2\text{CH}(\text{OH})\text{CH}_2\text{OSO}_3\text{Na}$ , have found wide application both for industrial and household use because of their excellent detergent properties. They may be made either by esterification of fatty acids in the presence of excess glycerin or by heating natural triglycerides with an excess of glycerin. The fatty acids most commonly used for the purpose are the mixed fatty acids from coconut oil. The resulting monoglycerides may be readily sulfated by the usual procedures. The most important commercial product of this class is made by Colgate-Palmolive-Peet Co. and sold under the trade names Arctic Syntax and Vel.

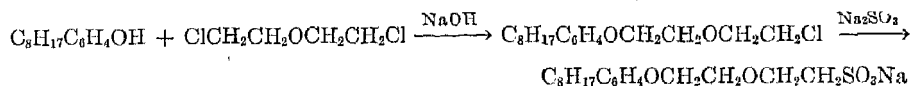
A somewhat unusual class of surface-active agents was developed in Germany before World War II and sold both there and in the U.S. under the name of Lamepons (45,48). They are condensation products of fatty acid chlorides with degraded proteins. Waste protein materials, such as scrap leather, are first broken down into lower polypeptides by heating with alkali (see *Protein hydrolyzates*), and the mixture is then acylated with a fatty acid chloride. The use of both oleoyl chloride and the acid chlorides of the coconut fatty acids is claimed. The acid chloride and caustic soda solution are run into the polypeptide mixture with good agitation in such a manner as to keep the reaction mass always alkaline. After the acid chloride has all been added, the temperature is raised to 60 to 70°C. to carry the reaction to completion.

The fatty acid chloride reacts with the primary amino group of the polypeptide forming a fatty acid-protein condensation product with a carboxyl group in the form of its sodium salt at one end. This leads to modified soaps which combine the properties of a fat with those of a protein, and which therefore not only have good resistance to hard water but are useful dispersing agents for lime soaps. They display good protective colloid action and are good emulsifying agents. On the other hand, they are very sensitive to acids and cannot be used at a pH much below seven.

Several series of widely used surface-active agents are derived from *diisobutylphenol* (*p*-(1,1,3,3-tetramethylbutyl)phenol), a compound made by alkylating phenol with diisobutylene. Diisobutylene, which is formed by the dimerization of isobutylene (2-methylpropene),  $\text{CH}_2=\text{C}(\text{CH}_3)_2$ , or by treating *tert*-butyl alcohol with 50% sulfuric acid, consists of a mixture of two isomers, 2,4,4-trimethyl-1-pentene and 2,4,4-trimethyl-2-pentene, in the ratio of about 4:1. If this mixture is condensed with phenol in the presence of sulfuric acid, the product is diisobutylphenol (44):



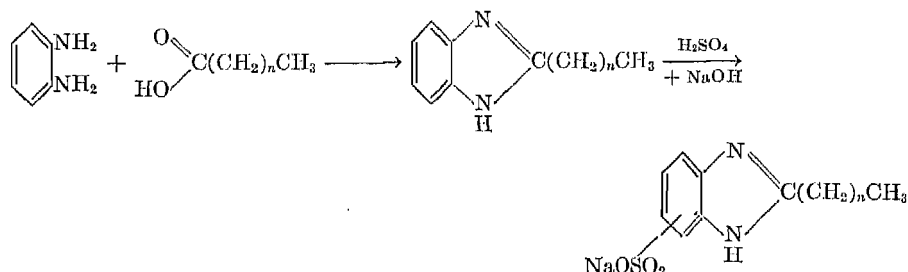
Because of its chain structure and the reactivity of the phenolic group, this compound is an excellent starting material for the preparation of either anionic, cationic or non-anionic surface-active agents. One of the procedures for making an anionic surface-active agent from diisobutylphenol is to react it with bis(2-chloroethyl) ether in the presence of caustic soda and then to replace the remaining chlorine atom with a sulfonate group by treatment with sodium sulfite:



Surface-active agents of this kind and others based upon diisobutylphenol were de-

veloped by Rohm and Haas Co. (50,52) and are marketed under the trade name Tritons.

In addition to aromatic nuclei, heterocyclic nuclei have also been used in surface-active agents (47). In this case 2-alkylbenzimidazoles are formed by condensing *o*-phenylenediamine or its derivatives with a fatty acid and then sulfonating the aromatic ring of the condensation product.



Compounds of this type are known as Ultravons and are produced commercially by Ciba Pharmaceutical Products.

A surface-active agent of the soap type, but with a modified fatty residue, was developed in Germany before World War II and was used extensively in that country during the war. It is known as Medialan A and is made by condensing a fatty acid chloride with sarcosine (*N*-methylglycine) and has the formula  $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}-(\text{CH}_2)_7\text{CON}(\text{CH}_3)\text{CH}_2\text{COONa}$ . It is said to have good detergent power and good resistance to hard water.



### Cationic Agents

Cationic surface-active agents are sometimes called "invert soaps" because their ionization is the reverse of that of the anionic surface-active agents of which soap is typical. In cationic compounds, the long-chain hydrophobic group becomes the cation and the anion is generally a chloride or bromide ion. With few exceptions, cationic surface-active agents are long-chain *quaternary ammonium salts* or salts of higher alkylamines. Cetyltriethylammonium chloride ( $[\text{CH}_3(\text{CH}_2)_{14}\text{CH}_2\text{N}(\text{C}_2\text{H}_5)_3]^+\text{Cl}^-$ ) (see p. 514) is typical of the cationic surface-active agents and closely resembles many of those on the market today. (See also Vol. 6, pp. 224, 226; Vol. 11, p. 315.)

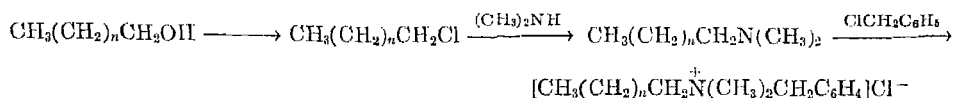
Several U.S. patents disclosing amine salts of condensation products of unsymmetrical diethylethylenediamine with carboxylic acids were issued to Hartmann and Kagi in 1925. One of these was the forerunner of later developments in this field (40). In 1929 a patent issued to the same inventors described quaternary ammonium salts of acyl derivatives of diethylethylenediamine (41). One important member of the series, the methoxysulfonate of oleoyldiethylmethylethylenediamine (diethylmethyl-(2-oleoamidoethyl)ammonium methyl sulfate),  $[\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{CONHCH}_2\text{CH}_2\text{NCH}_3(\text{C}_2\text{H}_5)_2]^+\text{OSO}_2\text{OCH}_3^-$ , together with the corresponding acetate and other salts, are produced by Ciba Pharmaceutical Products under the trade name Sapamines. They are excellent textile finishing materials.

In 1935 Domagk (5) reported the remarkable bactericidal power of a product called Zephirol toward a variety of pathogenic organisms. Zephirol, which is known as Zephiran in the U.S., is a mixture of alkylbenzyltrimethylammonium chlorides in which the alkyl chains are those present in the alcohols obtained by reducing the fatty



acids of coconut oil (see p. 524). These alcohols were the starting materials for the preparation of Zephrol.

Although Domagk did not disclose the method by which his compounds were prepared, there is good reason to believe that he used the following conventional procedures:



During World War II, Bond and Price found it possible to simplify the foregoing synthesis by using long-chain fatty amines as starting materials instead of fatty alcohols. Such amines are produced commercially in the U.S. from fatty acids, which are first converted to nitriles by heating them to above 300°C. in the presence of ammonia and then reducing the nitriles to primary amines. The mixed amines obtained in this manner from coconut oil fatty acids were methylated by treatment with formic acid and formaldehyde, and the resulting alkyldimethylamines, after neutralization with caustic soda, were quaternized by reaction with benzyl chloride. It is believed that this improved synthesis is now widely used for the preparation of alkylbenzyltrimethylammonium chlorides. Compounds of the class just described are produced by a number of firms and are sold under such trade names as Zephiran, Roccal, Rodalon, BTC and many others. They possess remarkably high bactericidal activity and their low toxicity makes them safe to use.

The striking success of the alkyldimethylbenzylammonium chlorides led to studies of the effect of changes in the structure of these compounds upon their germicidal activity. Kuhn, Jerchel, and Westphal (16) prepared a series of quaternary ammonium chlorides analogous to Zephiran but with two higher alkyl groups instead of only one methyl group. Carbon chains ranging from four to sixteen carbon atoms were included in the series.

If the condensation product of diisobutylphenol and bis(2-chloroethyl) ether (see p. 527) is condensed with dimethylamine in the presence of alkaline reagents, and the resulting tertiary amine reacted with benzyl chloride, a quaternary ammonium salt of high bactericidal activity is formed (53,55). This compound is sold under the trade names Hyamine by Rohm and Haas Co. and Phemerol by Parke Davis and Co.

Quaternary ammonium germicides are not restricted to compounds in which the nitrogen atom is present in a straight chain; it may also form part of a ring. Shelton and his co-workers (34) reported a series of quaternary ammonium salts derived from heterocyclic amines having a long hydrocarbon chain attached to the nitrogen, and showed that the compounds with a cetyl (*n*-hexadecyl) chain possessed the highest bactericidal activity. One member of this class is a well-known commercial product which is sold under the trade name of Ceepryn. According to Lawrence (17) this compound has a phenol coefficient of 350.

One disadvantage of cationic surface-active agents, either when used as such or as bactericides, is that they are incompatible with soaps or other anionic surface-active compounds. When anionic and cationic surface-active agents are brought together in solution, the large anion of the former reacts with the large cation of the latter producing a high-molecular-weight insoluble compound which usually precipitates out. Both compounds are thus inactivated. This is an important consideration in the

compounding of pharmaceutical preparations, or in using cationic germicides following the use of soap or cleaners containing anionic surface-active agents.

### Nonionic Agents

In the nonionics, the small, highly ionized hydrophilic group of the ionic agents is replaced by a long chain containing a series of weakly hydrophilic groups, such as ether linkages or hydroxyl groups. The repetition of weak hydrophilic groups has the same effect as one strong hydrophilic except that no ionization takes place. The case is analogous to that of the sugars which, although based upon a hydrocarbon structure, are completely water-soluble because of the large number of hydroxyl groups they contain.

The first nonionic surface-active agents were developed by I. G. Farbenindustrie in Germany (42,51) and were put on the market under the trade names of Peregals, Igepals, Leonils, and Emulphors. They were made by treating fatty alcohols or alkyl-substituted phenols with an excess of ethylene oxide, and have formulas such as  $\text{RO}(\text{CH}_2\text{CH}_2\text{O})_n\text{H}$ . Nonionic surface-active agents made in this way consist of two parts, a hydrocarbon residue and a polyethylene oxide chain. The latter makes up the hydrophilic group and gives the compound its solubility. From the nature of the reaction it will readily be seen that almost any number of compounds can be made, depending upon the type of hydroxy compound chosen and the number of moles of ethylene oxide used to react with it. The resulting compounds vary widely in physical appearance, solubility, and surface-active properties. It is thus possible to produce surface-active compounds with almost any desired characteristics. Certain structures favor detergency and others favor wetting, emulsification, and dispersion. Because of the flexibility of the reaction and the ease with which surface-active compounds of different properties can be produced by slight modifications in the procedure, the use of nonionics is increasing and they are competing with the anionics in many fields of application.

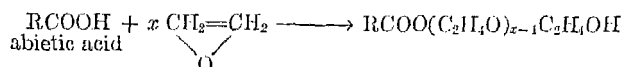
Nearly all of the nonionic surface-active agents on the market today are made by the reaction just described. A relatively insoluble compound (for the hydrophobic group) containing at least one hydroxyl group is reacted with ethylene oxide until the required solubility is obtained. The number of moles of ethylene oxide needed will depend upon the molecular weight and solubility of the hydrophobic group chosen. Typical of the hydrophobic groups used in the preparation of nonionics are fatty alcohols, alkyl-substituted phenols, fatty acids, rosin acids, and tall oil. Nonionic surface-active agents thus fall into two general classes, *ethers* and *esters*. Because ether types are extremely stable toward hydrolysis and are quite resistant to hard water, they find a wider field of application than do the esters.

A product typical of the ether class was manufactured in Germany under the name of Leonil OX by reacting oleyl alcohol with fifteen moles of ethylene oxide. The preparation of this compound is described by Hoyt (12). Analogous products using stearyl alcohol (1-octadecanol) and other fatty alcohols have also been made, but alkyl-substituted phenols seem to be the preferred starting materials for the preparation of the ether type of nonionic surface-active agents.

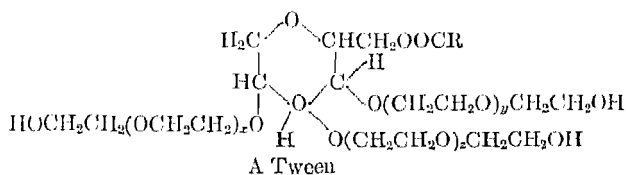
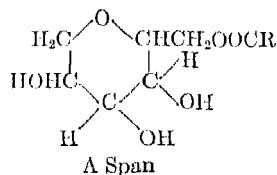
Polyethylene ether derivatives of alkyl phenols are widely sold under the trade name of Igepals. They were developed by I. G. Farbenindustrie in Germany and were among the first nonionic surface-active agents to be put on the market. A series

of similar products was developed by Rohm and Haas Co. in the U.S. by condensing diisobutylphenol (see p. 527) with ethylene oxide. They are sold under the trade name Tritons and are distinguished from the cationic and anionic compounds sold under the same trade name by different letters and numerals following the name.

In the preparation of esters by the ethylene oxide condensation reaction, compounds containing carboxylic groups are used as starting materials. Fatty acids, rosin acids, and tall oil, which consists of a mixture of fatty acids and rosin acids, have been successfully used. The Ethofats made by the Chemical Division of Armour and Co. are examples of the fatty acid types. Several well-known products of the rosin and tall oil types are sold under the trade names of Sterox and Renex. The reaction between ethylene oxide and abietic acid (see Vol. 11, p. 787), the principal constituent of rosin, is shown in the following equation:



In addition to the conventional ether and ester types of nonionic surface-active agents, others of somewhat more complex structures have also been commercially successful. Two classes of products known by the brand names of Spans and Tweens were developed by Atlas Powder Co. They are esters and ester-ethers derived from the anhydrides of hexahydric alcohols. The Spans are fatty acid esters of sorbitans (anhydrides of sorbitol) and the Tweens are fatty acid esters of sorbitans to which polyethylene ether chains have been attached by reacting them with ethylene oxide. The formulas for products of these types are:



(R = a fatty acid residue)

Two important classes of nonionics containing nitrogen are the Ethomids and Ethomeens, produced by the Chemical Division of Armour and Co. The Ethomids are fatty amides with two polyoxyethylene chains as substituents on the nitrogen atom, and the Ethomeens are long-chain amines with two polyoxyethylene chains on the nitrogen.

At least one sulfur-containing nonionic surface-active agent has been commercially successful. This is a thioether made by reacting *n*-dodecylmercaptan with ethylene oxide.

### Analysis and Testing

**Analysis.** Up to the present (1954), no simple, dependable methods for the identification and analysis of surface-active agents have been developed. The problem is difficult. There are more than a thousand different surface-active agents on the market. Even though these fall into as few as a dozen chemical classes, this does not simplify the problem as much as one might expect. Because they consist of mixtures, surface-active agents cannot be characterized by definite melting points, boiling points, or other physical constants. In addition, surface-active agents when free from in-

organic salts usually have a pasty or gelatinous consistency, do not crystallize readily, and are difficult to purify.

Several schemes for the identification of surface-active agents either alone or as ingredients of compounded detergents, have been published (20,24,39). These schemes are based upon the classification of the known surface-active agents and the use of group reactions to identify the various classes. Wurzschnitt (39) makes extensive use of microanalytical methods. The only elements occurring in surface-active agents are carbon, hydrogen, oxygen, nitrogen, sulfur, sodium, and chlorine. If, for example, it has been determined by elementary analysis that a given surface-active agent contains only carbon, hydrogen, and oxygen, it is limited to compounds containing carboxyl, ester, hydroxyl, or ether groupings. The first three groups may be determined by well-known reactions. But, if the tests for these groups are negative and the compound contains a high percentage of oxygen, then it may be assumed that it is an ethylene oxide condensation product of a fatty alcohol or a phenol.

This combination of elementary analysis and determination of functional groups may be extended to all classes of surface-active agents. By proper use of this method, the class to which any given compound belongs can be determined even though determination of the exact chemical structure may not be possible. For example, a dialkyl-naphthalenesulfonic acid may be readily identified as such although it may not be possible to determine the exact nature and positions of the alkyl groups. Such information can only be obtained by carrying out a difficult and time-consuming structure determination. It should also be pointed out that the above method requires that the sample be carefully purified if the elementary analyses are to have any meaning. Nevison, in a review of methods for the analysis of synthetic detergents (24), mentions that infrared and ultraviolet absorption spectra may be used to advantage in the analysis of surface-active agents. Here, too, a high degree of purity is required if the results are to be successful.

**Testing.** Carefully standardized empirical methods for measuring wetting power, detergency, and foaming have been in use for a long time. No more satisfactory method for measuring emulsifying power has been developed than that of using the emulsifying agent under test to make up emulsions and observing their stability. The same thing is true of the measurement of dispersing power for solid particles. In this case, however, the amount of sediment may be determined by a photoelectric turbidimeter. See also *Detergency*; *Emulsions*; *Foams*; and refs. 11, 19, 22, 29, 32, 35.

The most widely used method for measuring wetting power is the so-called Draves-Clarkson Test (6), which is the official method of the American Association of Textile Chemists and Colorists. It consists of measuring the time required for a 5-g. skein of gray cotton yarn to sink in a solution of the wetting agent. A small hook of copper wire weighing 3 g. is hooked through one end of the folded skein. To the other end of the wire hook a flat lead disk weighing about 40 g. is attached by means of a fine linen thread. A solution of the wetting agent is placed in a 500-ml. graduate and the skein with attached hook and sinker is allowed to drop into the solution and the stop watch started. The dry skein is at first buoyed up, but as the solution penetrates the yarn and it becomes wet, it sinks under the weight of the wire hook. The time is read just as the lower end of the hook touches the lead weight. The Draves sinking times for efficient wetting agents are only a few seconds at concentrations\* of 0.1–0.2%.

Another widely used test to evaluate the wetting power of surface-active agents is the so-called canvas disk test (10). In this test a 1-in. disk cut from standard duck

fabric is placed in a small funnel which is quickly inverted in the wetting agent solution so that the disk is held under the surface. As the liquid penetrates the fabric it sinks under its own weight. A stop watch is used to measure the time from the instant the funnel is inverted in the solution until the disk begins to sink. This test correlates quite well with the Draves test but in either test it is hard to obtain accurate sinking times below five seconds, and sinking times greater than a minute or two are likely to vary considerably from test to test. Sinking times are easiest to duplicate in the range from five seconds to one minute.

A number of methods have been devised for measuring the foaming characteristics of solutions of surface-active agents. The most satisfactory seems to be that of Ross and Miles (28). ASTM D1173-51T is very similar to this test. See also Vol. 2, p. 47, Vol. 6, p. 774.

The detergent power of a surface-active agent cannot be estimated simply by measuring a single physical property of one of its solutions, no matter how accurately this may be done. There is, however, a common belief that the ability of a compound to lower surface tension is evidence of its detergent power. For a discussion of detergency and the methods for evaluating detergents, see *Detergency*.

### Production

According to the Association of American Soap and Glycerine Producers, in 1945 the production of products containing surface-active agents amounted to 150,000,000 lb., and in 1952 it amounted to 1,700,000,000 lb., more than a tenfold increase in 10 years.

The U.S. Tariff Commission reports surface-active agents in terms of 100% content of active ingredients. The preliminary figure for total production for 1953 was 921,542,000 lb., an increase of 24% over the 741 million pounds reported for 1952. Sales in 1953 amounted to 732 million pounds, valued at \$145 million. The Tariff Commission classifies the surface agents as cyclic and acyclic (594 and 327 million pounds respectively for 1953) and gives a detailed breakdown within these groups. It also gives the following production figures for 1953: sulfated and sulfonated cyclic and acyclic compounds and acyclic salts of fatty acids (that is, mostly anion-active products), 751 million pounds; cyclic and acyclic nonsulfonated nitrogen-containing compounds (mostly cation-active), 58 million pounds; cyclic and acyclic esters and ethers (generally nonionic), in excess of 110 million pounds.

### Uses

The largest volume use of surface-active agents at present (1954) is in packaged household detergent mixtures. This application has developed almost entirely since World War II and accounts for the phenomenal growth in synthetic detergent production in recent years. Before the war almost the entire output of surface-active agents was used for industrial purposes, but it has been estimated that in 1954 industrial uses accounted for only some 20% of the production. The greatly increased use of surface-active agents has caused problems in sewage treatment (37). See also Vol. 12, p. 195.

The modern packaged household cleaners are mixtures of synthetic detergents and other substances that serve to improve their detergency. When they first entered the consumer field, they consisted of simple mixtures of about 40% surface-active

agent and 60% sodium sulfate. It was soon found, however, that the addition of complex phosphates, silicates, and certain other substances greatly improved the detergency of the mixtures. It has long been known in commercial laundry practice that the addition of alkaline substances (known as builders) to soap substantially improves its detergency. Caustic soda itself has been used, but for the most part builders consist of alkaline salts, such as carbonates, silicates, and phosphates. Since these alkaline salts are cheaper than soap, they not only improve detergency but lower the cost of the detergent.

When the synthetic detergents came into use in consumer products, the effect of builders was studied. The results proved to be so successful that almost all the present-day large-volume multipurpose household detergents are built with phosphates, silicates, and other ingredients to improve detergency and impart other desirable properties to the mixtures. Detergent mixtures compounded in this way are often called heavy-duty detergents. The builders in most common use today are the polyphosphates, tetrasodium pyrophosphate,  $\text{Na}_4\text{P}_2\text{O}_7$ , and sodium tripolyphosphate,  $\text{Na}_5\text{P}_3\text{O}_{10}$  (see Vol. 10, p. 413). These salts not only improve the cleansing power of the synthetic detergent, but act as water softeners by sequestering calcium and magnesium ions. This is one of the reasons that the modern packaged detergents are so much more effective than soap in hard water areas. Although synthetic detergents do not form insoluble precipitates with the metallic ions of hard water, they do function more efficiently in soft water.

The fatty alcohol sulfates are outstanding detergents but are relatively expensive. On the other hand, the alkylarenesulfonates, though inferior to the fatty alcohol sulfates in detergency, are cheaper, and if made from the right raw materials, can be made to exhibit good detergent power. It has also been found advantageous to use mixtures of these two types.

The major ingredients in the present-day all-purpose household cleaners are synthetic detergents and builders, but in recent years it has become the practice to add small quantities of other substances to improve their detergency, particularly for clothes washing. One such additive is sodium carboxymethyl cellulose, which has the property of preventing dirt from redepositing upon fabrics after it has been removed by the detergent solution. Another additive in common use is one of the so-called optical bleaches or white dyes (see *Stilbene dyes*; *Whitening agents*). These have the property of absorbing ultraviolet radiation and emitting a blue fluorescence in the visible region. The result is to mask the yellow cast often present on fabrics and to give them a brighter appearance. Ordinary blueing has long been used for the same purpose, but has the disadvantage of absorbing some light, whereas the optical bleaches actually cause the fabric to reflect more light.

Surface-active agents are important in the textile industry, being used in large amounts in scouring, kier boiling, and other steps. (See *Textile technology*.) Both anionic and nonionic agents have been used in the scouring of wool, and acid-stable wetting agents of the alkylarenesulfonate type are used in carbonizing wool to promote wetting of the wool by the acid. Surface-active agents are used in kier boiling to promote wetting of the cotton and to prevent channeling of the solution. Both ionic and nonionic agents are used, including fatty alcohol sulfates, alkylarenesulfonates, and nonionics. In bleaching surface-active agents are used as wetting agents. In this application they must resist the action of the bleaching agent. Sulfated fatty alcohols and the Igepon type of agent are among those used. Other applications in

processing include use in removing sizing, lubricating oils, natural waxes, and similar materials. They are also used in dye baths to aid penetration and act as levelling agents. The agent used for each purpose depends on many factors, and the choice is frequently a matter of trial and error. See also ref. (30).

The use of surface active agents in metal cleaning is increasing. In alkaline cleaning solutions, surface-active agents are used to aid wetting, dispersion, and emulsification, especially of nonsaponifiable materials. As in textile technology, the agent to be used must usually be determined by trial. In some applications a nonfoaming agent is necessary. In strongly alkaline solutions which are heated continuously, agents containing ester linkages or other groups unstable in alkaline solution are unsuitable. Nonionic agents are particularly useful in those cleaners which use an electric current in cleaning. (See *Metal surface treatment; Electroplating.*) In addition to cleaning for such industrial processes as plating, surface-active agents are used in cleaning metals for appearance, sanitation, and other purposes. In this application the cationic agents are also used as bactericides.

Surface-active agents are used in ore flotation to modify the surface of the mineral selectively, making it hydrophobic, and they are also used as frothing agents (see *Flotation*). Surface-active agents are used widely in insecticidal sprays to suspend solid ingredients where they are present and to emulsify mineral oil. They also promote spreading and thus enhance the toxic effect of the mixture. Many surface-active agents themselves also possess insecticidal properties.

Surface-active agents have many other uses, and the number of uses is rapidly increasing. But, as Ackley (1) has pointed out, the selection of the right compound involves difficulties in almost every case. These difficulties can only be resolved by consultation with the manufacturer and by careful experimentation on the part of the user.

### Bibliography

- (1) Ackley, R. R., *Ann. N.Y. Acad. Sci.*, **46**, 511-29 (1946).
- (2) Adkins, H., *Reactions of Hydrogen with Organic Compounds over Copper-Chromium Oxide and Nickel Catalysts*, University of Wisconsin Press, Madison, 1937, p. 97 (footnote).
- (3) American Association of Textile Chemists and Colorists, *Technical Manual and Yearbook*, **29**, 90-91 (1953).
- (4) Caryl, C. R., *Ind. Eng. Chem.*, **33**, 731-37 (1941).
- (5) Domagk, G., *Deut. med. Wochschr.*, **61**, 829-32 (1935).
- (6) Draves, C. F., and Clarkson, R. G., *Am. Dyestuff Repr.*, **20**, 109-16 (1931); cf. also (3).
- (7) Dreger, E. E., Keim, G. I., Miles, C. D., Shedlovsky, L., and Ross, J., *Ind. Eng. Chem.*, **36**, 610-17 (1944).
- (8) Fischer, E. K., and Gans, D. M., *Ann. N.Y. Acad. Sci.*, **46**, 371-404 (1946).
- (9) Gotte, E., *Kolloid Z.*, **64**, 222-27, 327-31, 331-35 (1933).
- (10) Harris, J. C., *Detergency Evaluation and Testing*, Interscience, N.Y., 1954.
- (11) Harris, J. C., Kamp, R. E., and Yanko, W. H., *ASTM Bull.*, **158**, 49-52 (May 1949) cf. also (9).
- (12) Hoyt, L. F., P.B. 3868, Office of Technical Services, Dept. of Commerce, Washington, cf. also (29).
- (13) Ipatieff, V. N., Pines, H., and Schmerling, L., *J. Org. Chem.*, **5**, 253-63 (1940).
- (14) Kastens, M. L., and Peddicord, H., *Ind. Eng. Chem.*, **41**, 438-46 (1949).
- (15) Killeffer, D. H., *Ind. Eng. Chem.*, **25**, 138-40 (1933).
- (16) Kuhn, R., Jerchel, D., and Westphal, O., *Ber.*, **73**, 1095-1100 (1940).
- (17) Lawrence, C. A., *Surface-Active Quaternary Germicides*, Academic Press, N.Y., 1950, p. 64.
- (18) Lenher, S., *Chem. & Ind.*, **60**, 497 (1941).
- (19) Linford, H., and Saubestre, E. B., *Plating*, **38**, 713-17; 847-65 (1951).

- (20) Linsenmeier, K., *Melliand Textilber.*, **21**, 468-69 (1940).
- ✓(21) McCutcheon, J. W., *Synthetic Detergents*, MacNair-Dorland Co., N.Y., 1950.
- (22) Morgan, O. M., and Lankler, J. G., *Ind. Eng. Chem., Anal. Ed.*, **14**, 725-26 (1942).
- (23) Neville, H. A., and Jeanson, C. B., III, *J. Phys. Chem.*, **37**, 1000-08 (1933).
- (24) Nevison, J. A., *J. Am. Oil Chemists Soc.*, 576-82 (1952).
- (25) Price, D., *Ann. N.Y. Acad. Sci.*, **46**, 407-24 (1946).
- (26) Price, D., *Detergents, What They Are and What They Do*, Chemical Publishing Co., N.Y., 1952.
- (27) Price, D., *Soap Sanit. Chemicals*, **29**, 54-57; **77** (1953); cf. also (25).
- (28) Ross, J., and Miles, G. D., *Oil & Soap*, **18**, 99-102 (1941).
- (29) Sanders, H. L., and Lambert, J. M., *J. Am. Oil Chemists Soc.*, **27**, 153-59 (1950).
- (30) Schwartz, A. M., and Perry, J. W., *Surface-Active Agents*, Interscience, N.Y., 1949.
- (31) *Ibid.*, pp. 57-58.
- (32) Seyferth, H., and Morgan, O. M., *Am. Dyestuff Repr.*, **20**, 525-32 (1938).
- (33) Sharrah, M. L., and Feiyhner, G. C., *Ind. Eng. Chem.*, **46**, 248 (1954).
- (34) Shelton, R. S., et al., *J. Am. Chem. Soc.*, **68**, 757-59 (1946).
- (35) Spring, S., Forman, H., and Peale, L. F., *Ind. Eng. Chem., Anal. Ed.*, **18**, 201-04 (1946).
- (36) Symposium on Synthetic Detergents, Division of Industrial and Engineering Chemistry, American Chemical Society, 125th National Meeting, Kansas City, Mo., 1954. See *Chem. Eng. News*, **32**, 1319 (1954).
- (37) Symposium on Water and Water Treatment Problems Involving Detergents, Division of Water, Survey, and Sanitation Chemistry, American Chemical Society, 119th National Meeting, Cleveland, Ohio, 1953. See *Chem. Eng. News*, **31**, 1072 (1953).
- (38) Venkataraman, K., et al., *J. Soc. Dyers Colourists*, **53**, 91-100 (1937); *ibid.*, **54**, 465-72 (1938); *ibid.*, **55**, 125-34 (1939); *ibid.*, **57**, 41-49 (1941).
- (39) Wurzschnitt, B., *Chem. Ztg.*, **74**, 16-20 (1950).
- (40) U.S. Pat. 1,527,868 (Feb. 24, 1925), M. Hartmann and H. Kagi (to Ciba).
- (41) U.S. Pat. 1,737,458 (Nov. 26, 1929), M. Hartmann and J. Kagi (to Ciba).
- (42) U.S. Pat. 1,970,578 (Aug. 21, 1934), C. Schoeller and M. Witwer (to I. G. Farbenindustrie).
- (43) U.S. Pat. 1,981,792 (Nov. 20, 1934), J. W. Orelup.
- (44) U.S. Pat. 2,008,017 (July 16, 1935), W. F. Hester (to Rohm and Haas).
- (45) U.S. Pat. 2,015,912 (Oct. 1, 1935), F. Sommer (to Grunau, Landshoff u. Meyer).
- (46) U.S. Pat. 2,028,091 (Jan. 14, 1936), A. O. Jaeger (to American Cyanamid).
- (47) U.S. Pat. 2,036,525 (Apr. 7, 1936), C. Granacher (to Ciba).
- (48) U.S. Pat. 2,041,265 (May 19, 1936), L. Orthner and G. Meyer (to I. G. Farbenindustrie).
- (49) U.S. Pats. 2,088,014-21 (July 27, 1937), J. N. Wickert et al. (to Union Carbide).
- (50) U.S. Pat. 2,098,203 (Nov. 2, 1937), H. A. Bruson (to Rohm and Haas).
- (51) U.S. Pat. 2,111,820 (Mar. 22, 1938), A. Steindorff and C. Platz (to I. G. Farbenindustrie).
- (52) U.S. Pat. 2,115,192 (Apr. 26, 1938), H. A. Bruson (to Rohm and Haas).
- (53) U.S. Pat. 2,170,111 (Aug. 22, 1939), H. A. Bruson (to Rohm and Haas).
- (54) U.S. Pat. 2,176,423 (Oct. 17, 1939), A. O. Jaeger (to American Cyanamid).
- (55) U.S. Pat. 2,229,024 (Jan. 21, 1941), H. A. Bruson (to Rohm and Haas).
- (56) "Bibliographical Abstracts of Methods for Analysis of Synthetic Detergents," Special Technical Publication 150, A.S.T.M., Philadelphia, 1953.
- (57) Sisley, J. P., *Encyclopedia of Surface Active Agents* (P. J. Wood, translator), Chemical Publishing Co., N. Y., 1952.
- ✓(58) *Soap Sanit. Chemicals*, **28**, No. 7, 48-57 (1952); No. 8, 52-63 (Aug. 1952); No. 9, 52-61 (Sept. 1952); No. 10, 50-61 (Oct. 1952).
- (59) "Synthetic Detergents" Card Index Service, J. W. McCutcheon, 475 Fifth Avenue, New York, N.Y.

DONALD PRICE



## SURFACE PROPERTIES

A knowledge of the theory of surface properties is of great importance in such fields as detergency (*q.v.*), emulsions (*q.v.*), and flotation (*q.v.*), and in understanding the behavior of surface-active agents (*q.v.*). See also *Colloids; Thermodynamics*.

**Fundamental Concepts.** The region of contact between two phases is an interface. Interfaces are the special topic of investigation of surface chemistry. If one of the phases is a gas, and the pressure is so low that the effect of the molecules in the gas phase can be neglected, the system is called a surface. The feature that differentiates molecules in an interface from those in the contiguous phase is that these molecules are in an asymmetric molecular field. This asymmetric field leads to a change in interatomic distance and the energetics of the system. Both kinetic and equilibrium properties have been investigated. Since nearly all the work has been concentrated on the equilibrium state, and the kinetics are little understood, this article is devoted exclusively to the equilibrium state.

Two general approaches have been used in the study of interfaces: thermodynamic and mechanical. In the former, attention is focused on the changes in the quantities of thermodynamic interest: free energy, enthalpy, entropy, volume, etc., caused by the introduction of an interface into the system under consideration. In the mechanical approach, the interface is considered an additional vector function that must be considered for a complete description of the system. Both methods have their advantages in that each yields a solution to certain questions more readily than the other. When the same problem is solved by both techniques, it is obvious that the same answer is obtained.

A feeling of many of the ideas and procedures in surface chemistry can be obtained from a consideration of the following model. Let us consider a semi-infinite, perfect, monatomic crystal, bounded by the [100] plane at 0°K. In addition, let us assume that the interatomic distance and the zero-point energy are independent of position, and that the potential energy is pair-wise additive. In this model, we can consider that all the atoms lie in planes parallel to the surface of the crystal. If  $a$  is the distance between nearest neighbors, there will be  $1/a^2$  atoms per sq.cm. For simplicity, we can compute the potential energy of the system in which the unit of length is  $a$ . If  $\phi(r)$  is the energy of interaction of two atoms  $r$  units apart, the energy of interaction,  $\phi(i)$ , of an atom in the interior of the crystal with all the atoms in a plane  $i$  layers away is:

$$\phi(i) = \sum_{x=-\infty}^{\infty} \sum_{y=-\infty}^{\infty} \phi(i^2 + x^2 + y^2) \quad (1)$$

The total potential energy of this atom, in the interior,  $\phi_B$ , is:

$$\phi_B = \phi(0) + 2 \sum_{i=1}^{\infty} \phi(i) \quad (2)$$

The potential energy of an atom in the  $i$ th layer of the surface,  $\phi_s(i)$ , is:

$$\phi_s(i) = \phi(0) + 2 \sum_{j=1}^{i-1} \phi(j) + \sum_{j=i}^{\infty} \phi(j) \quad (3)$$

Now, if by some means the surface of the crystal is increased in area by 1 sq.cm., the change in potential energy,  $\Delta\phi_s$ , is:

$$\Delta\phi_s = \sum_{i=1}^{\infty} i\phi(i) \quad (4)$$

Equation (4), first derived by Born and Stern (8), is the result we wish to discuss.

Equation (4) shows that the number of atoms associated with an interface is indefinite. Consequently, the only definite unit of measurement is the extent of interface rather than the mole. Many investigators discuss the depth of the surface or interfacial region. This at best can only be an approximation and is meaningless unless the property and degree of approximation considered are specified. For example, if we consider the depth of the surface region with respect to energy, we find that for solid or liquid argon it is 3 layers thick (48,59) and for sodium chloride 30 layers thick (51) to an approximation of 99%. On the other hand, if we consider the electronic perturbation of the atoms, we find that in both of the above cases the effect is confined almost completely to the first layer (54).

From the manner in which the surface potential energy was obtained, it can be seen that the surface or interfacial property is a difference. This leads to two important conclusions. First, if the particle becomes small enough, the energy becomes a function of size. To date, this region has not been experimentally accessible, but several formulas have been derived (11,39,60). A second conclusion is that a single molecule cannot possess a surface energy. This follows from the fact that the surface energy is a difference. Consequently, one can only rigidly discuss surface or interfacial properties for phases in contact.

The preceding model is oversimplified. First, there is a variation in interatomic distance at the surface. This is a quantity which no one has as yet succeeded in measuring. Second, the system was such that only one phase and only the zero-point motion of the atoms was present. This leads to a rather sharply defined surface. The usual state is where there are two phases and the molecules have an appreciable thermal motion. These two factors lead to a smearing out of the atomic positions. Thus, the interface is a transition region between the two phases. Through this transition region it is possible to draw surfaces in which the time-average density of each species of molecules is constant. The density varies from surface to surface. This variation in density is an unsolved problem. Somewhere in this region, the actual dividing surface exists, provided that what is meant by dividing surface is specified.

From the preceding, the interface is not a well-defined region in the sense that there is a sharp surface of demarcation. Rather there is a more or less gradual transition in properties from one phase to another. The degree of fuzziness of this region, and its extent, depend upon the composition and temperature of the system.

**Experimental Procedures.** The measurement of most importance for the vapor-liquid and liquid-liquid interface is the measurement of the surface tension (6,14,24). This quantity is a free energy. Consequently, if the surface or interfacial energy is determined as a function of temperature, many quantities of thermodynamic interest can be obtained from the results of the measurements. On insoluble films on aqueous systems (1,12,13,27,28,31,35,36) surface potential and viscosity measurements are of great value.

The most usual measurement on the solid-vapor interface is that of adsorption (10). The measurement yields an approximate quantity of the change in free energy

of the system. The values are not sufficiently good to obtain good values of the other thermodynamic functions. Fortunately, it is possible to make direct calorimetric measurements so that these quantities can be determined by the combination of the two techniques.

On liquid-solid systems, the measurement of the contact angle and the heat of wetting (6,9,30,55) are of value. The contact angle is the angle made by the tangent to the liquid with the solid ( $\theta$ , Fig. 1). The measurement is made through the liquid.

The greatest technical importance of this quantity lies in the flotation of minerals. In order for flotation to occur, it is necessary that the contact angle be other than zero. The technical problem in flotation is the addition of an agent that makes the contact angle other than zero against the desired ore and zero against the gangue. There is no theory available at the present time which enables the *a priori* solution of this problem.

One word must be said concerning the experiments involving interfaces. The properties of interfaces can be very sensitive to traces of impurities. Utmost pre-

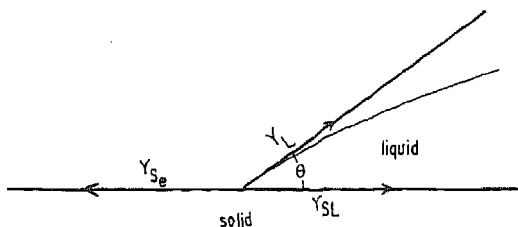


Fig. 1. Contact angle of a liquid against a solid.

cautions must be taken in the purification and the prevention of accidental contamination. For example, the heats of wetting of titanium dioxide in water and in dry benzene are 520 and 180 ergs per sq.cm., respectively. If the same measurement is made in benzene saturated with water, the result obtained is 510 ergs per sq.cm. for all practical purposes the same as that obtained in water (24). The reason for this extreme sensitivity is that on the order of  $10^{-9}$  moles is usually sufficient to completely change 1 sq.cm. of interface.

**Thermodynamics.** There has been an extensive development of the thermodynamics of surface and interfaces. Gibbs (18) and Guggenheim (19,20) have presented long and systematized treatments. The thermodynamics involving interfaces differs from ordinary thermodynamics by the addition of a new variable involving the surface. This means that there is one additional variable in a general equation of state. If the thermodynamic quantities are considered per unit area, then the equations have the same number of independent variables as if the interface was absent.

For a system involving an interface, instead of the usual thermodynamic relationship  $dE = p dV - T dS$  we can write:

$$dE = p dV + A d\gamma + \sum_{i=1}^{i=n} \mu_i dN_i - T dS \quad (5)$$

where  $A$  is the area of the interface,  $\gamma$  the surface tension,  $N_i$  the mole fraction of the  $i$ th species, and  $\mu_i$  the chemical potential  $(\partial F / \partial N_i)_{T,p}$  (free energy per mole). By

the usual thermodynamic techniques, nearly all the desired relations can be obtained from this equation. For a one-component system we can write:

$$(\partial F / \partial A)_{T,p} = \gamma \quad (6)$$

where  $F$  is the Gibbs free energy,  $A$  the area of the system, and  $\gamma$  the surface tension. The entropy per unit area,  $s$ , is:

$$s = -(\partial \gamma / \partial T)_p \quad (7)$$

and the enthalpy per unit area,  $h$ :

$$h = \gamma - Ts \quad (8)$$

The heat capacity,  $Cp_s$ , due to the interface is:

$$Cp_s = -T(\partial^2 \gamma / \partial T^2)_p \quad (9)$$

The change in volume,  $\Delta V$ , due to the formation of 1 sq.cm. of interface is:

$$\Delta V = (\partial^2 \gamma / \partial p)_T \quad (10)$$

The fugacity,  $f$ , of a liquid in a spherical drop of radius  $r$  is obtained from the fugacity,  $f_0$ , of a large volume of liquid by:

$$RT \ln \frac{f}{f_0} = \frac{2\gamma \bar{V}}{r} \quad (11)$$

where  $\bar{V}$  is the molar volume.

All the above formulas are of value except that for the volume change (eq. 10). If the pressure is increased on a system, the solubility of the gas changes, and the measurements are not made on the same system as the pressure is changed (56).

It was indicated above that the surface tension was a function of the particle size. The equation of Buff (11) is:

$$\gamma = \gamma_0 \left( 1 - \frac{2\delta_\infty}{r} + \dots \right) \quad (12)$$

Where  $\delta_\infty$  is the difference in superficial density of the liquid with a planar surface and with radius  $r$ . Other treatments are also available (39,60).

The above equations are sufficient for the treatment of pure liquid systems, or the interface between two insoluble liquids. In the latter case, the interfacial tension is substituted for the surface tension. The measurement that is made is the surface tension as a function of temperature.

The determination of the surface tension of solids has not been completely solved. At the present time there is a great interest in both theoretical and experimental procedures. An experimental procedure has been devised and applied by Jura and Garland to the determination of this quantity for magnesium oxide (42,43). Some pertinent comments have been made by Bauer (4). The method of Jura and Garland depends upon the determination of the enthalpy (41) and the heat capacity as a function of particle size. The results of Giauque (16) are also utilized. The equations are:

$$h_{298} = \Delta H / A \quad (13)$$

$$h_T = h_{298} + \frac{1}{A} \int_{298}^T \Delta Cp \, dT \quad (14)$$

$$s = \frac{1}{A} \int_0^T \frac{\Delta C_p}{T} dT \quad (15)$$

$$\gamma = h - Ts \quad (16)$$

All the symbols have their usual significance.

Equation (6) can also be used for the development of the thermodynamics of multicomponent systems. The most important single equation for the treatment of multicomponent systems is the Gibbs adsorption equation:

$$-d\gamma = \sum \Gamma_i d\mu_i \quad (17)$$

At constant temperature and pressure, the equation can be written:

$$-d\gamma = RT \sum \Gamma_i d \ln f_i \quad (18)$$

In equation (17) the only undefined term is  $\Gamma_i$ , which has the dimensions moles per sq.cm. In the interface, the concentration of the various components is not the same as that in either of the phases.

$\Gamma$  is defined as the difference in number of moles in the interfacial region and in the bulk. Mathematically:

$$\Gamma_i = C_B - C_S \quad (19)$$

where  $C_S$  is the number of moles in the surface and  $C_B$  in the bulk. This change in concentration is called adsorption. Adsorption may be either positive or negative. If the adsorption is positive, the species is said to form a film.

By an arbitrary choice of the dividing surface, we can make  $\Gamma$  of any species equal to zero. For a two-component system the equation then becomes:

$$\Gamma = - \frac{1}{RT} \left( \frac{\partial \gamma}{\partial \ln f} \right)_{T,p} \quad (20)$$

This equation can be applied to any two-component system. If we deal with a liquid solution, the adsorption of the solute can be obtained from a measurement of the surface tension and concentration. As an example of such a treatment, the reader is referred to the data of Harkins and Wampler (37) for solutions of *n*-butyl alcohol in water. If a gas is physically adsorbed on the surface of a solid,  $\Gamma$  and  $p$  are measured. The integration of the equation gives:

$$\Delta\gamma = \pi = RT \int_0^p \Gamma d \ln p \quad (21)$$

In this way, the change in surface tension of the solid can be determined as a function of the amount of gas that is adsorbed. If we have an insoluble film on water, the surface tension and amount adsorbed are measured, and the change in fugacity of the film-forming material can be obtained by integration (3,45).

Koenig (49) has shown how the equation can be extended to treat three-component systems. His results are especially useful for solutions.

Since the interfacial properties are difference functions, the statistical treatment of interfaces can be no better than the treatment of the bulk. In the liquid state, the problem is complicated by the fact that the distribution function of the atoms in the interface is not known. The relatively poor results for the surface tension obtained by

the most rigorous treatments are due to the ignorance of this function. The best treatment is that of Buff and Kirkwood (48). Their final result is of the form:

$$\epsilon = \frac{2\pi N_0^2}{V} \int g(r) \phi(r) r^2 dr \quad (22)$$

where  $\phi(r)$  is the distribution function, and  $g(r)$  the potential function. Other treatments (22,42) are not as good as that quoted earlier.

Molecular and ionic solids have been treated at 0°K. Shuttleworth has made computations of the molecular crystals, while Born (7) and Lennard-Jones and co-workers in particular have extended these measurements (51,52). Any attempt to extend these measurements to higher temperatures must await the development of methods to compute the heat capacity as a function of both temperature and particle size. The work of Montroll (53) and Jura and Pitzer (47) can be used to give adequate values of the desired surface thermodynamic quantities to about one-hundredth of the Debye temperature of the solid. This range is not of practical interest. Another statistical treatment worthy of mention is that of Guggenheim (21), who treated the surface tension of liquids at the critical temperature.

**Theory of Capillarity.** This phase of the subject is purely mechanical. Its practical importance stems from the fact that it is the basis for all the static methods of surface tension determinations. Conceptually, there also is great importance associated with this particular phase of the subject. In this treatment, the surface is considered as a vector tangent to the surface. Since the surface is curved, there is a pressure difference that must be considered as well as the effect of the gravitational field.

Since the interface is so indefinite, the question arises as to the position of the surface tension vector, the value of the vector being a function of position; that is, the vector would have a different magnitude on every surface through the interface. Recently, it has been shown that if the vector is placed on the surface where  $\Gamma = 0$ , the magnitude of this vector is equal to the measured value of the surface tension, and is equal in magnitude to the surface free energy discussed in the preceding section. A similar problem arises in the treatment of the surfaces of solids.

The fundamental equation of the theory of capillarity is the Laplace equation:

$$\Delta p = \gamma \left( \frac{1}{R_1} + \frac{1}{R_2} \right) \quad (23)$$

where  $\Delta p$  is the pressure difference,  $\gamma$  the surface tension, and  $R_1$  and  $R_2$  the principal radii of curvature. This is a differential equation which is in general nonintegrable for the imposed boundary conditions. Any static method of surface tension determination must be based on the Laplace equation if it is to yield reliable results.

The capillary-height method is the only method in which the equation has been sufficiently extensively studied in order to obtain a result that is rigorously correct. To illustrate the general method, the rigorous treatment of the capillary-height method is outlined. The pressure difference is  $\rho gh$ , where  $\rho$  is the difference in density of the liquid and the atmosphere,  $g$  the value of the gravitational constant at the position of the experiment, and  $h$  the rise (positive or negative) of the liquid in the capillary. If  $(rh)^{1/2}$  is greater than about  $10r$ , it can be shown that the surface is for all practical purposes spherical. Under these circumstances, the two radii of curvature

are equal, and each equals  $r/\cos \theta$  where  $r$  is the radius of the capillary, and  $\theta$  is the angle of contact. The formula for the capillary height method then is:

$$\gamma = \rho g r h / 2 \cos \theta \quad (24)$$

One other problem must be mentioned, the measurement of  $h$ . It is apparent that the measurement to the meniscus is not completely accurate, since the liquid above the meniscus contributes to the hydrostatic pressure. Several formulas have been proposed for this correction (24). The experimental problems associated with the capillary-height method are stringent. Consequently, even though the basic theory is the most completely developed, the method is used primarily as a standard, and as a means of checking on other methods of surface tension methods. The complete details of the methods can be obtained in the papers of Richards and Carver (57), Harkins and Brown (29), and Gross and Young (21,24). The last authors have developed the method to the point that they obtained a precision of 0.01%.

The derivation of the formulas for surface tension measurements other than the capillary-height method cannot be obtained in such simple terms. Consider the contour of a drop of liquid hanging from a circular tip. This is illustrated in Figure 2. If the origin is placed at the center of the tip, the Laplace equation yields the differential equation:

$$\frac{\rho g y}{\gamma} = \frac{d^2 y / dx^2}{[1 + (dy/dx)^2]^{3/2}} + \frac{dy/dx}{x[1 + (dy/dx)^2]^{1/2}} \quad (25)$$

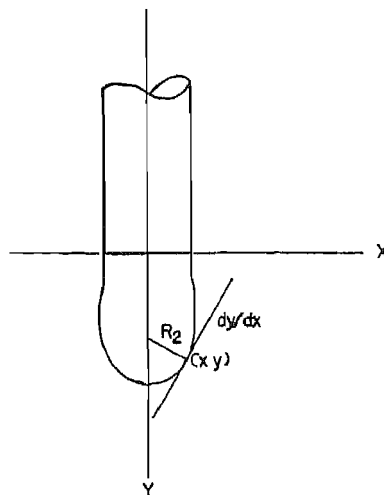


Fig. 2. Profile of a drop suspended from a circular tip.  $R_1$  is the radius of curvature in the plane of the paper. The length of  $R_2$  is shown. Note that in this case the  $y$  axis is considered positive in the downward direction.

This equation, first derived by Lohenstein, is nonintegrable. It is obtained for many different sets of boundary conditions.

Bakker (2) has presented the most extensive treatment of the Laplace equation and related problems. Bashforth and Adams (5) have prepared tables of the results of numerical integrations of the equation. Freud and Freud (15) have made a partial integration for the ring method of surface tension determination. For details of the many available methods for surface tension determination see ref. 6,14,24.

**Films in Liquid Solutions.** Adsorption of a solute to form a film occurs with most nonionic solutions in water. The formation of the film is evidenced by the reduction of the surface tension. A typical example is the system *n*-butyl alcohol in water.

Solutions of nonaqueous systems have been studied. In these systems, the variation of the surface tension is usually rather small. Theories of solutions have been extended to treat the surface tensions of systems of this kind (38).

**Films on Solids.** Measurement of the adsorption of a gas on the surface of a solid is capable of yielding the change in surface free energy. There are two auxiliary

measurements that are of importance for the solid, the measurement of the contact angle of a liquid, and of the heat of wetting of the solid in the liquid. For the detailed development of the thermodynamics, reference should be made to the papers of Hill (40).

Several techniques are available for the determination of contact angles (6). The contact angle gives a relationship between the liquid-solid interface, the liquid-vapor interface, and the solid-vapor interface. The relationship usually given is:

$$\gamma_{se} = \gamma_{SL} + \gamma_L \cos \theta \quad (26)$$

where  $\gamma_{se}$  and  $\gamma_{SL}$  are the interfacial tensions of the solid saturated with the vapor of the liquid and of the solid-liquid interface, respectively. The present writer has never seen a rigorous derivation of this equation. The only point of note in the above relationship is  $\gamma_{se}$ . This quantity is the surface free energy of the solid with the adsorbed film of the vapor on the surface. It is not the free surface energy of the solid (34). Theoretically, the importance of this measurement is that it permits the computation of solid-liquid interfacial computations from those obtained from a study of the solid-vapor interface.

The heat of wetting is important in that it permits the direct determination of the enthalpy of solid-liquid interfaces. The necessary condition for this type of experiment is that the solid be completely insoluble in the liquid. If  $h_s$  is the enthalpy of a solid-liquid interface, and  $h_{SL}$  that of the solid in equilibrium with its own vapor, then the heat of wetting  $h_w$ , is (1):

$$h_w = h_{SL} - h_s \quad (27)$$

If  $n$  moles of the vapor of the liquid are adsorbed on the surface of the solid before immersion in the liquid, the enthalpy is  $h_w$ . It can be readily seen that the heat of adsorption,  $\Delta H_A$ , of  $n$  moles of vapor on the surface is (32):

$$\Delta H_A = H'_I - H_I + n\lambda \quad (28)$$

where  $H'_I$  and  $H_I$  are the heats of melting of the clean solid and that with  $n$  moles on the surface, respectively, and  $\lambda$  is the heat of vaporization.

If the solid is saturated with the vapor before immersion in the liquid, and the contact angle is zero, then the area of the solid covered with the film is (33):

$$A = \Delta H_e/h_L \quad (29)$$

where  $\Delta H_e$  is the heat of immersion of the solid saturated with the vapor and  $h_L$  is the surface energy of the liquid.

If the solid is nonporous, this is essentially the true area of the solid. This technique for the determination of the enthalpy also has an advantage over direct calorimetry in that it gives coverages not conveniently accessible by direct calorimetry.

**Spreading.** The formation of a film on a surface is termed spreading. The term is usually restricted to those systems in which there is a decrease in the surface tension, and where the spreading material is insoluble in the subphase. There are two major points of interest in spreading: the mechanism by which spreading occurs, and the conditions under which spreading takes place. The subphase may be either solid or liquid. Obviously, the spreading occurs because there is a decrease in the free energy of the entire system. For the time being this can be accepted as a necessary condition.

The actual process of spreading may take place in one of two ways: the molecules



of the spreading material may diffuse over the surface from the position in which it is concentrated, or spreading may occur through the vapor phase—the molecules vaporize and then are adsorbed on the surface of the solid. It is apparent that the latter type of spreading can be important only when the vapor pressure of the spreading material is appreciable. It is also possible that in certain systems the spreading process can occur by both mechanisms. If octadecyl alcohol is placed on the surface of pure water, it is apparent that spreading must take place by surface diffusion. The usual adsorption experiments are spreading experiments in which the spreading occurs completely through the gaseous phase. If a drop of water is placed on a graphite crystal in a closed system, it is likely that the spreading of the water on the graphite occurs by both methods.

The time required for spreading is thus obviously determined by the means whereby the spreading occurs. Such studies have not been sufficiently carefully analyzed so that any real conclusions can be drawn from the few available data. It is also apparent that two important factors in the rate of spreading are the surface tension of

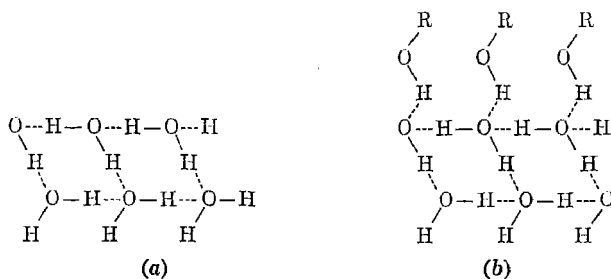


Fig. 3. Highly idealized drawings of (a) the surface of water, (b) a higher alcohol on the surface of water.

the original material and the surface tension of the system in the final state. The consequence of the last statement is that we would expect more extensive and rapid spreading when the surface tension of the original system is high. We would expect a given molecule to spread more rapidly on mercury than on water, and more rapidly on water than on an organic liquid, for example benzene. The liquid of most general interest is water.

Of equal importance to the mechanism of spreading and the theoretical aspects of the phenomenon is the structure and nature of the molecules that spread. Since water is the most important substance in this respect, this discussion is restricted to water, but the arguments can be readily extended to any other liquid or solid subphase. First it is necessary to look at the structure of water itself (see Fig. 3a). The most important feature is that there is hydrogen bonding between the molecules giving each hydrogen a coordination number of 2 and each oxygen a coordination number of 4, except at the surface. Thus, if another molecule is to enter into this structure, it must break the hydrogen bonds that exist in the water itself.

If the material which is to spread can also form hydrogen bonds, then energetically it will be relatively easy for this material to substitute itself in the surface for a water molecule. Thus, we would expect that the organic molecules which would spread most easily are the alcohols, carboxylic acids, and the nitrogen-containing compounds that still have one hydrogen attached to the nitrogen atom. If there is attached to the functional group a residue which is of such a nature that it is insoluble in

water, then the functional group can bond itself in the water and the residue will remain outside. In general, the residue will have a lower surface tension than the water, and the net result will be a reduction of the surface tension of the surface. This also is a necessary condition for spreading. In Figure 3(b), a highly schematic representation of a higher alcohol on the surface of water, it may be noted that the surface oxygens now have a coordination number of 4. This can be done without changing the remaining structure, and the hydrogen bonding is maintained.

On the above grounds it would be expected that molecules that do not hydrogen bond would spread only slightly. Actually there is no situation where the spreading would be incomplete. The extreme of nonspreading can be illustrated with ethyl chloride on water. The amount of spreading which occurs here is so slight that it becomes almost immeasurable. A class of molecules that might be expected to spread, but which appear not to, are the very long-chain molecules with but a single functional group. Thus, the 30-carbon alcohols and acids appear not to spread in spite of the fact that the molecules satisfy the necessary criteria. In these cases it is apparent that the cohesion of the chains has become so great that spreading will not occur. That is, a third criterion must be included, namely, that the ratio of functional groups to the number of methylene groups cannot be too low. There appears to be no hindrance to spreading as long as the number of methylene groups is of the order of 20 or 24 times the number of function groups present. Summarizing: if spreading is to occur (by spreading is meant here an appreciable reduction in the surface tension of water), the following conditions must be satisfied: First, the molecule must have a functional group that is capable of forming a reasonably strong hydrogen bond. Second, the molecule must have a residue that has a low surface tension. Third, the molecule must have one functional group for roughly 20 methylene groups.

The only theoretical considerations of spreading are those of classical thermodynamics. There are two kinds of films, duplex and nonduplex. In the former, the film can be thought of as being sufficiently thick that its properties are the sum of an interfacial tension between two condensed phases and the film-vapor interface. For example, a duplex film of benzene on water would be of such a nature that its properties would be the sum of those of the benzene-water interface and the benzene-vapor interface. A nonduplex film would be any other kind of film; with a few exceptions these are monomolecular.

If a duplex film is to be formed, the necessary conditions are:

$$\gamma_A + \gamma_{AB} < \gamma_B \quad (30)$$

where  $\gamma_A$  and  $\gamma_B$  are the surface tensions of *A* and *B* respectively, and  $\gamma_{AB}$  the interfacial tension. The conditions for the formation of a nonduplex film are:

$$\gamma_A + \gamma_{AB} > \gamma_B \quad (31)$$

These problems have been discussed in detail by Harkins (25).

### Bibliography

- (1) Adam, N. K., *Physics and Chemistry of Surfaces*, Clarendon Press, Oxford, 1941.
- (2) Bakker, O., *Kapillarität und Oberflächenspannung*, Akademische Verlagsgesellschaft, Leipzig, 1928.
- (3) Bangham, D. H., *Trans. Faraday Soc.*, **33**, 805 (1937).

- (4) Bauer, S. H., *J. Am. Chem. Soc.*, **75**, 1004 (1953).
- (5) Bashforth, F., and Adams, J. C., *An Attempt to Test the Theories of Capillary Action*, Cambridge Univ. Press, London, 1883.
- (6) Bikerman, J. J., *Surface Chemistry for Industrial Research*, Academic Press, N.Y., 1947.
- (7) Born, M., *Encyklopedie der math. Wiss.*, **5**, 743 (1923).
- (8) Born, M., and Stern, O., *Sitz. preuss. Akad. Wiss.*, 901 (1919).
- (9) Boyd, G. E., and Harkins, W. D., *J. Am. Chem. Soc.*, **64**, 1190 (1942).
- (10) Brunauer, S., *The Adsorption of Gases and Vapors*, Princeton Univ. Press, Princeton, N.J., 1943.
- (11) Buff, F., *J. Chem. Phys.*, **12**, 1591 (1951).
- (12) Copeland, L. E., and Harkins, W. D., *J. Chem. Phys.*, **10**, 272 (1942).
- (13) Dervichian, D. G., *J. Chem. Phys.*, **7**, 932 (1939).
- (14) Dorsey, N. E., *Natl. Bur. Standards Sci. Papers*, **21**, No. 540 (1926).
- (15) Freud, B. S., and Freud, H. F., *J. Am. Chem. Soc.*, **52**, 1772 (1930).
- (16) Giauque, W. F., *J. Am. Chem. Soc.*, **71**, 3192 (1949).
- (17) Gross, P. L. K., *The Theory of Atomic Collision, the Determination of a Standard for Surface Tension Measurements* (Ph.D. Thesis), University of Chicago, 1926.
- (18) Gibbs, J. W., *The Collected Works of J. Willard Gibbs*, Vol. I, Longmans, Green, N.Y., 1931.
- (19) Guggenheim, E. A., *Thermodynamics by the Method of J. Willard Gibbs*, Methuen, 1933.
- (20) Guggenheim, E. A., *Thermodynamics*, Interscience, N.Y.-London, 1949.
- (21) Guggenheim, E. A., and Fowler, R. H., *Statistical Thermodynamics*, University Press, Cambridge, England, 1939, p. 401 ff.
- (22) Haisima, *Proc. Phys. Math. Soc. Japan*, **22**, 825 (1940).
- (23) Harkins, W. D., *Physical Chemistry of Surface Films*, Reinhold, N.Y., 1952.
- (24) Harkins, W. D., "Determination of Surface and Interfacial Tension," in Weissberger, A. (ed.), *Physical Methods of Organic Chemistry*, Vol. I, 2nd ed., Interscience, N.Y.-London, 1949.
- (25) Harkins, W. D., *J. Chem. Phys.*, **9**, 552 (1941).
- (26) Harkins, W. D., *J. Am. Chem. Soc.*, **39**, 541 (1917).
- (27) Harkins, W. D., and Anderson, T. F., *J. Am. Chem. Soc.*, **59**, 2189 (1937).
- (28) Harkins, W. D., and Boyd, G. C., *J. Phys. Chem.*, **45**, 20 (1941).
- (29) Harkins, W. D., and Brown, F. E., *J. Am. Chem. Soc.*, **41**, 499 (1919).
- (30) Harkins, W. D., and Dahlstrom, R., *Ind. Eng. Chem.*, **22**, 897 (1930).
- (31) Harkins, W. D., and Fisher, E., *J. Chem. Phys.*, **1**, 852 (1933).
- (32) Harkins, W. D., and Jura, G., *J. Am. Chem. Soc.*, **66**, 919 (1944).
- (33) Harkins, W. D., and Jura, G., *J. Am. Chem. Soc.*, **66**, 1362 (1944).
- (34) Harkins, W. D., and Livingston, H. K., *J. Chem. Phys.*, **10**, 342 (1942).
- (35) Harkins, W. D., and Myers, R. J., *J. Phys. Chem.*, **40**, 959 (1936).
- (36) Harkins, W. D., and Nutting, G. C., *J. Am. Chem. Soc.*, **61**, 2040 (1939).
- (37) Harkins, W. D., and Wampler, R. W., *J. Am. Chem. Soc.*, **53**, 850 (1931).
- (38) Hildebrand, J. H., and Scott, H., *Solubility of Nonelectrolytes*, Reinhold, N.Y., 1950.
- (39) Hill, T. L., *J. Chem. Phys.*, **18**, 246 (1950).
- (40) Hill, T. L., *J. Am. Chem. Soc.*, **72**, 3923 (1950).
- (41) Johnson, F. M. A., Lipsett, S. G., and Moos, O., *J. Am. Chem. Soc.*, **50**, 2071 (1928).
- (42) Jura, G., *J. Phys. & Coll. Chem.*, **52**, 40 (1948).
- (43) Jura, G., and Garland, C., *J. Am. Chem. Soc.*, **74**, 6033 (1952).
- (44) Jura, G., and Garland, C., *J. Am. Chem. Soc.*, **75**, 1006 (1953).
- (45) Jura, G., and Harkins, W. D., *J. Am. Chem. Soc.*, **66**, 1356 (1944).
- (46) Jura, G., Loesser, E. H., Bosford, P. R., and Harkins, W. D., *J. Chem. Phys.*, **14**, 117 (1946).
- (47) Jura, G., and Pitzer, K. S., *J. Am. Chem. Soc.*, **74**, 6030 (1952).
- (48) Kirkwood, J., and Buff, F., *J. Chem. Phys.*, **17**, 338 (1949).
- (49) Koenig, F. O., *J. Chem. Phys.*, **18**, 449 (1950).
- (50) Langmuir, I., *J. Am. Chem. Soc.*, **39**, 1848 (1917).
- (51) Lennard-Jones, J. E., and Dent, B. E., *Phil. Mag.*, **8**, No. 7, 530 (1929).
- (52) Lennard-Jones, J. E., and Taylor, P. A., *Proc. Roy. Soc. (London)*, **109**, 476 (1925).
- (53) Montroll, E., *J. Chem. Phys.*, **18**, 183 (1950).
- (54) Nathans, M., and Jura, G., unpublished.
- (55) Razouls, R. I., *J. Phys. Chem.*, **45**, 910 (1941).
- (56) Rice, O. K., *J. Chem. Phys.*, **15**, 333 (1947).
- (57) Richards, T. W., and Carver, E. K., *J. Am. Chem. Soc.*, **43**, 827 (1921).

- (58) Rideal, E. K., *An Introduction to Surface Chemistry*, University Press, Cambridge, England, 1926.  
(59) Shuttleworth, R., *Proc. Physical Soc. London*, **62**, 167 (1949).  
(60) Tolman, R. C., *J. Chem. Phys.*, **17**, 333 (1949).

GEORGE JURA

**SURFACTANTS.** See *Surface-active agents*.

## SURGICAL DRESSINGS

The term surgical dressings applies in general to absorptive materials that are used in surgical operations and for wound care. With the advent of plastic-type dressings, the term should be broadened to cover all absorptive materials used in surgery and absorptive and nonabsorptive materials used for protection and treatment of wounds or other bodily injuries.

Surgical dressings are made chiefly from cellulosic materials. Although there is a growing market for various dressings containing plastic materials, the all-plastic dressings are still in the early developmental stages. The cellulosic materials used in dressings include mainly cotton, rayon, wood pulp, and paper. These materials are used in surgical dressings because they are low in cost, highly absorptive, nonreactive to tissues, easily purified, and steam-sterilizable.

Representative surgical dressings include gauze bandages, gauze sponges, cotton-filled dressings, sanitary napkins, roll cotton, cotton balls, adhesive tape, medicated dressings, and many other items. Surgical dressings may be further classified from the standpoint of the manufacturer into sterile and nonsterile dressings. In general, surgical dressings for hospitals (bulk items) are sold nonsterile (with a few exceptions) and dressings (packaged in units) sold at retail to the consumer are presterilized. In addition, there is a growing industrial and institutional market for all types of surgical dressings.

### Physical and Chemical Properties

The physical properties of the materials used (cotton, wood pulp, for example) largely determine the various specific applications for which surgical dressings are used and their construction. In general, *dressings for wounds* must wet rapidly and have a high capacity for holding fluids, that is, they should remove fluids rapidly from their source and pass them into the interior of the dressing. They should also be soft in order to give maximum protection without irritation. *Bandages* should have tensile strength and conformability and should not slip. *Plaster of Paris bandages* (splints or casts) are designed for rigidity, tensile strength, conformability, and setting time. In *adhesive tapes*, tensile strength and adhesiveness are most important.

The chief chemical properties to be desired in surgical dressings are those of inertness and lack of irritation in use. Cellulosic materials when properly purified are nonirritating and inert. Special care must be given to the selection of nonirritating materials for the adhesives on adhesive tapes and bandages. Medicated dressings, such as those containing iodoform, are usually designed with specific uses in mind.

### Manufacture

The procedures used for manufacturing surgical dressings are dependent on the materials being processed.

#### TYPES OF DRESSINGS

**Surgical cottons** are made from lint cotton (ginned virgin cotton), comber cotton, cotton linters, and various types of processed cotton materials which are available on the market. (See also *Cellulose*, Vol. 3, p. 352; *Cotton; Cottonseed*, Vol. 4, p. 587.) Lint and comber cottons are used primarily where higher-quality longer fiber cottons are needed. Cotton linters and processed cotton materials generally find use as low-cost filler materials in dressings.

All cottons must be thoroughly processed before they can be used in surgical dressings. Lint cotton contains varying amounts of leaf and stem material which is removed by mechanical opening and cleaning equipment. Linters must also be cleaned thoroughly. Other grades of cotton may or may not be mechanically cleaned, depending on the foreign matter present.

The cleaned cotton materials are then boiled and bleached by rigorously controlled chemical processing (2). In the boiling process, the cotton is treated with a 1-2% sodium hydroxide solution containing soap (or detergents) and a sequestering agent, such as tetrasodium pyrophosphate, at temperatures of 200-250°F. for 1-3 hr. This treatment removes much of the natural waxes and oils and also softens and disintegrates any foreign matter that may remain after the cleaning operation. The boiled cotton is absorbent but not of good color. It is then washed with water and bleached with chemicals such as hydrogen peroxide or sodium hypochlorite. The bleaching not only whitens the cotton but also improves its wetting properties and assists in disintegration of any remaining foreign materials. After boiling and bleaching, the cotton is dried and then picked and carded or garnetted on equipment similar to that used in textile mills.

*Roll cotton* (purified cotton, absorbent cotton, U.S.P. XIV) is prepared by superimposing and gathering together the webs from several cards in order to yield a product of required bulk and weight. Single card webs are condensed or gathered into slivers which are used in making *cotton balls* or *cotton-tipped applicators*, which are made on special high-speed equipment and are packaged either in bulk or in unit packages. *Lower-grade cottons* and *nonabsorbent cottons* (unboiled and unbleached) are used as fillers and backings, respectively, for dressings, such as *sanitary napkins* and *dressing combines* (gauze-covered cotton-filled dressing pads). These cottons may be handled on garnetts after being picked, in order to obtain the dressing filler in the desired form and at high production rates.

**Creped cellulose** (paper) is widely used in such surgical dressings as disposable diapers, underpads, breast pads, dressing combines, and sanitary napkins. Creped cellulose for use in surgical dressings must possess special properties, such as rapid wetting after being steam-sterilized, good aging properties, high fluid-holding capacity, softness, high bulk, and sufficient tensile strength for handling on high-speed machines. It is made up in rolls of suitable width and in single or multiple plies for specific products.

In some cases, a nonabsorbent creped cellulose is needed, as for center or side strips in sanitary napkins. This paper differs from the absorbent cellulose described

above in that the sheets must be tight (no holes) and be treated with chemicals, such as resin size or wax emulsions to develop nonabsorbent properties.

**Surgical gauze** (absorbent gauze, sterile absorbent gauze, U.S.P. XIV) is prepared from gray goods of various thread counts. The counts most frequently encountered are 14x10, 18x14, 20x12, 28x24, 44x36, and 64x56. The lower-count gauzes (20x12 and lower) are used for surgical sponges and for covering dressings such as sanitary napkins and dressing combines. In these cases, the relatively low tensile strength of the gauze is not an important factor. The higher-count gauzes (28x24 and higher) are used for bandages and special applications, such as making crinoline for adhesive bandages and back plasters. Surgical gauzes are made to conform to U.S.P. specifications for such properties as thread count, weight, tensile strength, wetting time, ash content, and pH. In order to meet these specifications, special boiling and bleaching techniques are necessary (see p. 549). After boiling and bleaching, surgical gauze is essentially pure cellulose (*q.v.*), freed of natural oils, waxes, and other foreign materials. The boiling and bleaching process is important also in that it should impart the necessary properties for the gauze to be handled on the high-speed machines used to convert it into finished products. The gauze is then dried to proper width on tenter-type dryers. The dried gauze is slit or cut into rolls of proper width for use in making final products.

*Gauze bandages*, U.S.P. XIV, are made from the higher-count gauzes (28x24, 32x28, and 44x36) by slitting the tentered rolls to proper width and length on slitters. The bandages are then packaged on automatic machines.

Lower-count gauze (20x12, U.S.P. Type VII) is generally used in making *gauze sponges* or *pads*. Rolls of gauze of proper width are fed into special machines which cut and fold the gauze into sponges. Gauze sponges are made in various sizes, such as 2 by 2 in., 3 by 3 in., 4 by 4 in., and 4 by 8 in., varying numbers of plies from 8 to 32. *Cotton-filmed gauze sponges* are made in a manner similar to regular gauze sponges except that a thin film or web of cotton is placed on the gauze before the sponge is formed in the machine. The cotton-filmed sponge is lower in cost than the all-gauze sponge and has a greater fluid-holding capacity. *Cotton* and *creped cellulose filler* sponges are lowest in cost. These sponges have a very high absorptive capacity because the creped paper acts to spread the absorbed fluids throughout the interior of the dressing.

*X-ray-detectable gauze sponges* are made on machines which are identical to gauze sponge machines. An x-rayable filament or insert made of heavy-glass fibers or of plastic material containing barium sulfate, U.S.P. XIV, or other x-ray-absorbing chemicals is sealed to the gauze before the sponge is folded. Such sponges may be detected by x-ray equipment if left in the patient after an operation.

**Medicated surgical dressings**, a large group, are generally made from gauzes which are impregnated with various medicinals, such as iodoform, N.F. IX, tyrothricin, U.S.P. XIV, N.N.R., merbromin, N.F. IX (Mercurochrome), sulfathiazole, U.S.P. XIV, and other antibacterial materials (see *Antiseptics*). Such medicated gauzes are generally prepared by using a simple impregnation process which is modified as necessary to suit the materials being treated. In most cases, the solution of the medicinal material is made up to the proper strength in a supply tank, and the proper type of surgical gauze is then impregnated using a combination of dip tank and mangle roll, which is set to attain the proper pickup of the medicinal material on the gauze. The wet gauze coming from the mangle is generally passed into a tenter or other type

of dryer, such as that generally used in the handling of textile materials. The medicated gauzes may then be slit to the proper width and used in the preparation of various types of medicated dressings, such as adhesive bandages and gauze pads.

**Oxidized cellulose**, U.S.P. XIV, N.N.R. (oxycellulose, Oxycel—see Vol. 3, p. 344; Vol. 7, p. 421), is another specialty-type surgical dressing. Oxycellulose is prepared by oxidizing surgical gauze with nitrogen dioxide gas,  $\text{NO}_2$ . The oxycellulose gauze is cut to the proper size and packed in closed containers, such as glass vials, and then sterilized. Oxycellulose, when properly prepared, is a hemostatic material and is gradually absorbed by bodily fluids when it is used to pack wounds.

**Adhesive tape** (adhesive plaster; sterile adhesive plaster; U.S.P. XIV), an important item in surgical dressings, consists basically of a backing material with pressure-sensitive adhesive (see Vol. 1, p. 199) spread on one side. Different kinds of backing materials are used in the preparation of adhesive tapes for various applications. The adhesive tape most commonly used is generally made from a type of print cloth having a thread count of approximately 80x80. Such a fabric has the required amount of tensile strength and will tear easily in the crosswise direction, so that when the proper amount of tape has been used it can be severed in this manner from the supply roll. Other backing materials are made from various types of elastic fabric, used in applications where constriction should be avoided, various plastic films, and waterproofed or coated cotton fabrics. The techniques used for preparing and applying the pressure-sensitive adhesive mass to the backing material are very similar to those used in the preparation of other pressure-sensitive adhesive products. After the pressure-sensitive materials have been properly compounded, they are spread onto the backing in most cases by either calendering or solvent-spreading techniques. The large supply rolls of the finished product are slit into various widths and wound on cores or spools, etc., as the application requires.

**Adhesive bandages** (adhesive absorbent bandages, U.S.P. XIV; adhesive absorbent compress; adhesive absorbent gauze, U.S.P. XIII) are pressure-sensitive-type bandages containing an element designed to absorb the fluid coming from a wound and designed for use on minor wounds, such as small cuts, scratches, and burns. They are made in varying widths, lengths, and shapes for various applications. Adhesive bandages are generally prepared on high-speed machines of many types of design.

In general, supply rolls of the various components of the adhesive bandage are fed in proper sequence into the machine as the adhesive bandage is being made. A roll of adhesive tape of the proper type is first fed into the machine. The first operation is usually the punching of vent holes at regular intervals to serve for aeration when the finished bandage is in use. Narrow strips of gauze are then fed into the machine at the proper point from supply rolls, folded together to form the absorbent member of the adhesive bandage, cut into small portions, and placed over the vent holes. Strips of facing material, such as crinoline, plastic materials laminated to paper, or plastic films of various types (cellophane, cellulose acetate, polyethylene), are then applied to cover the gauze pad and the adhesive mass. The continuous strip of material passing through the machine is then cut to length and placed automatically on the paper, into which it is wrapped. Various types of wrappings are used and may be sealed around the adhesive bandage by such techniques as gluing or heat-sealing. Since adhesive bandages are generally sold as individually wrapped sterile items, it is essential that tight seals be achieved on all packages, and that the paper used for packaging be such

that the maximum degree of protection against recontamination is achieved. Glassine-type papers, either plain or heat-sealable, are most often used; they are very dense and practically impervious to bacteria. Other types of paper and various types of films such as cellophane and polyethylene may also be employed.

**Nonwoven fabrics** (see *Textile technology*), because of low cost and softness, are more and more coming into use in surgical dressings. They are made from cotton or mixtures of cotton and rayon or other fibers. These fabrics are used as covers for products such as sanitary napkins, dressing combines, disposable diapers, and under-pads.

**Elastic bandages** are important where the use requires the bandage to give some bodily support, as in sprains. These bandages are relatively high in cost as they are made from relatively heavy-weight specially woven fabrics, some of which may contain rubber-covered yarns. Elastic bandages may be stretched 25-30% over their unstretched length and conform well to body contours. Their sturdy construction permits numerous launderings and re-uses.

Among the more recently developed surgical dressings are the all-purpose protective dressing and the conforming bandage, which were developed to be used together in the treatment of large-area wounds, principally burns. The **all-purpose protective dressing** is generally made in sizes capable of being used on either the limbs or the trunk of the body and is essentially a thick pad of absorbent material having an impervious backing. Once applied to a wounded area, it is usually left in place for a period of 10 days to 2 weeks. The dressing as now manufactured has a surgical gauze facing, to be applied directly to the wounded area, under which is a thick layer of absorbent cotton followed by an equally thick layer of absorbent creped cellulose paper. This is followed by several layers of repellent cellulose paper and finally by a water-resistant backing material. The absorbent cotton in the dressing acts as a wick in rapidly absorbing fluids which are exuded from the wounded area. The fluids are transferred from the cotton to the creped cellulose, which acts to spread the fluid throughout the interior of the dressing. This combination of paper and cotton aids in maintaining a dry condition at the surface of the wound at all times. The **conforming bandage** is used to keep the all-purpose protective dressing in place. Many types of conforming bandages are suitable for this purpose. The bandage should be made from a material having elastic properties so that the dressing can be held tightly against the wounded area at all times, as such a bandage must give easily in case the wounded member swells or contracts in size. Conforming bandages are made at present by mercerizing a low-count gauze, such as 20x12, and keeping the gauze at all times in a relaxed condition. The mercerization is accomplished by treating the gauze with a 13-22% sodium hydroxide solution and allowing the gauze to shrink freely. The gauze is then washed free of sodium hydroxide, keeping it relaxed at all times, and dried and slit to the proper width and length. Bandages produced in this manner will have a stretch of 35 to 50% of their length. When the stretched bandage is allowed to relax, a large part of the stretch is recoverable.

There are many **specialty items**, such as *operating room caps, face masks, sanitary napkin belts, laparotomy packs, triangular bandages*, and *hemostatics (q.v.)* such as fibrin foam, N.N.R., and absorbable gelatin sponges, U.S.P. XIV, N.N.R. (see also *Blood fractionation*). Many of these products require hand cutting, sewing, and other operations and are made so that they can be re-used many times, thus costing more to make than disposable items, such as cotton balls and gauze sponges.



## STERILIZATION

It has been standard practice in the surgical dressings industry for many years to sterilize most of the surgical dressings which are sold in the retail market. Although many other techniques have been suggested, the common practice is to effect such sterilization (*q.v.*) under steam pressure at elevated temperatures. Alternative processes described in the literature include the use of ethylene oxide gas, formaldehyde, propylene oxide, and other chemical materials; electron beams, high- and low-voltage x-rays, and radioactive materials. When steam under pressure is used, the products to be sterilized must be properly packaged so that the steam will penetrate the package in order to allow sterility to be achieved and sterility can be maintained after the process has been completed. Many problems can occur which have to be faced in the selection of packaging materials and the design of packages which are both economical and most suitable for the consumer to use.

The packaged materials are placed on trays or trucks and put into the steam autoclave. After the autoclave chamber has been sealed, the air is removed by means of a vacuum pump and steam is introduced into the chamber. The temperature employed to achieve sterilization generally ranges from 230 to 250°F. and is maintained for periods of 30 min. up to 1 to 2 hr., depending on the conditions necessary to achieve sterility. When the proper length of time at the specified temperature has been completed, the steam is removed from the chamber and replaced with air filtered through a filter capable of removing all bacteria, which also cools the product in the autoclave. The materials are then removed and sent to areas where they are packaged for shipment.

## Bibliography

- (1) Cook, E. F., and Martin, E. W. (eds.), *Remington's Practice of Pharmacy*, 10th ed., Mack Publishing Co., Easton, Pa., 1951, pp. 1259-67.
- (2) Mauersberger, H. R. (ed.), *Matthews' Textile Fibers*, 6th ed., Wiley, N.Y., 1954.

O. S. PLANTINGA

## SURGICAL SUTURES

In the practice of surgery a strand or fiber used to sew together tissues, nerves, or blood vessels is referred to as a *suture*; when used to ligate or "tie off" a blood vessel to prevent hemorrhage, it is known as a *ligature*. The word "suture" will be used in this discussion to refer to both sutures and ligatures.

Suture materials are divided into two general classes, absorbable and nonabsorbable.

## Absorbable Sutures

**Absorbable surgical suture**, U.S.P. XIV (surgical gut, U.S.P. XIII, surgical catgut, catgut suture), is a strand prepared from collagen derived from healthy animals, purified, rendered sterile, and protected from contamination. It is the only completely and readily absorbable suture material and is the most widely used. Absorbable sutures are absorbed or digested during the healing process, by the tissues in which they are embedded. Their function is to serve as either a suture or a ligature

until such time as body repair has progressed to the point where they are no longer needed.

The manufacture of catgut dates back to ancient days. In 200 A.D. Galen, the Greek surgeon, wrote of the use of gut sutures on Roman gladiators. The modern catgut period started with the paper of Joseph Lister in *Lancet* (1869), "Observations on Ligature of Arteries on the Antiseptic System."

Modern catgut is usually obtained from the submucous connective tissue of the small intestine of healthy sheep. The actual technical methods of preparing the intestine vary in different countries, and a good deal of secrecy surrounds them. Briefly, the intestines are cleaned of their contents and split longitudinally into two ribbons. To facilitate removal of foreign tissue, a 0.5% sodium carbonate solution is used. A series of mechanical scraping operations remove the mucosa, muscularis, and serosal layers, leaving only the submucosa.

The submucosa appears as a thin, strong network consisting chiefly of collagen fibers. Subsequent processing increases the orientation of these collagen fibers and develops the strength of the strand. From one to four such ribbons, depending upon the diameter of the catgut which is to be produced, are stretched while still wet and spun under controlled tension. The number of twists per inch is predetermined to produce the best possible bonding of the ribbons. The strands are then dried under tension, polished, and cut into appropriate lengths for tubing and sterilization.

Raw gut, called *plain*, is chemically similar to rawhide. Tanned or *chromicized catgut* is somewhat similar to chrome-tanned leather. Tanning (usually with chromium salts, such as ammonium dichromate) lowers the rate of digestion of catgut by body enzymes during the healing of a wound. Deficient tanning of catgut may result in its premature absorption, with possible wound disruption. Excessive chrome concentrations may produce sutures that are extremely slow to digest and may remain in normal tissue as a foreign body for many months.

The tanning or chromicization process is applied either to the submucosa ribbons before being twisted into the strand form, or to the finished dried strand. In one method the ribbons or strands are immersed for varying lengths of time in a bath containing chromium salts in such concentration as to yield final chrome contents ranging from 0.1 to 2% calculated as  $\text{Cr}_2\text{O}_3$ .

The U.S.P. XIV recognizes four types of catgut: *Type A*, plain or untreated, is a strand of collagen which has not been treated in any manner that will alter its normal rate of digestibility; *Type B*, mild treatment; *Type C*, medium treatment; and *Type D*, prolonged treatment, are strands which have been tanned or otherwise treated so that they will resist digestion for progressively longer periods of time.

Various attempts to produce "synthetic" catgut have been made because the quality of sheep intestines varies and the process of making catgut is a long, tedious, and complicated one. In one synthetic process the corium of animal hides or skins is soaked in acid, pH 2-4, for 16-24 hours at 10-30°C., the excess liquid drained off, and the corium put through a meat grinder. With gentle heating the ground material is centrifuged and filtered, giving a concentrated solution of collagen. This solution is diluted to 5-15%, deaerated *in vacuo*, extruded through a spinneret, and then immersed in a coagulating bath (35% ammonium sulfate or magnesium sulfate at pH 7.8) at 20-30°C. The washed filament is air-dried and may be tanned for greater resistance to absorption (5).

Unfortunately, none of the synthetic catgut strands has a wet tensile strength comparable to that of natural catgut.

*Sterilization and Tubing of Catgut.* Catgut must be sterile, supple, strong, and absorbable. Many unsuccessful attempts to sterilize gut by means of chemicals, such as phenol and mercuric chloride, have resulted in the use of heat as the generally accepted method of sterilization (*q.v.*). However, the process is not simple. Normally holding 15–20% moisture, the catgut must be dried before a high temperature is applied, otherwise the water present in it would cause partial hydrolysis with almost complete loss of tensile strength. The sterilizing temperature is critical, less than 150°C. being insufficient for consistent sterility and more than 155°C. tending to cause brittleness. The heat must be applied evenly throughout the strand.

The customary procedure is for the catgut to be coiled and placed in tubes open at one end in which the gut is dehydrated and sterilized by a method whereby the required temperature and time of exposure can be closely controlled. After sterilization one of two procedures may be followed to give either nonboilable or boilable sutures.

*Nonboilable sutures* are prepared by introducing a sterilized 90–95% alcoholic reconditioning fluid and instantly sealing the open end of each tube hermetically. Because of the water present in the reconditioning fluid the outside of the tube cannot be sterilized by heat before use. It is usually sterilized by storage at room temperature in containers of alcoholic formaldehyde.

*Boilable sutures* are dried and sealed in an anhydrous tubing fluid, such as xylene, to avoid damage to the catgut during boiling or steam sterilization. The disadvantage of boilable catgut is that the necessary drying produces a stiff, brittle, and wiry strand which requires reconditioning in water before it can be used by the surgeon. Correct reconditioning is a difficult procedure to control in the operating room. These sutures are becoming obsolete.

#### OTHER ABSORBABLE SUTURES

**Kangaroo tendons** are obtained from the split tail tendons of the wallaby species of kangaroo. They are processed in a manner similar to nonboilable catgut and may be used plain or chromicized. The tendons consist of compact fibrous bundles of connective tissue, which are characterized by a relatively low affinity for water, so that presoaking of such tendons before use is of prime importance. Kangaroo tendons vary in length from about 10 to 17 in. or over and are supplied in fine, medium, and coarse strands in sealed glass tubes. They are fairly resistant to tissue enzymes and are still sometimes used to suture the broken ends of bones, support fracture lines, and effect the cure of hernia, the last being the principal use of the finer-gauge tendons.

**Fascia lata** is composed of strips taken from the fibrous tissue which covers the thigh muscles of beef cattle. Its principal use has been to strengthen abdominal fascia in the repair of hernia. Fascia lata is supplied in sterile tubes in strips  $\frac{1}{8}$  in. wide and 8 in. long.

**Cargile membrane** is a thin sheet of pliable tissue obtained from the appendix of beef cattle. It is designed primarily to cover surfaces from which the peritoneum has been removed, especially where a sterile membrane would lessen the formation of adhesions. This membrane is available in sterile sheets about 4 by 6 in.

**Insultic membrane**, prepared from the allantoic membrane of bovine embryos, has been used similarly to cargile membrane but is now becoming obsolete.

### Nonabsorbable Sutures

Nonabsorbable surgical suture, U.S.P. XIV (surgical sutures, surgical silk, and sterile surgical silk, all U.S.P. XIII), is defined as a strand of material that effectively resists enzymic digestion in living material and consists of strands of metal or organic material produced from other than segments of connective tissue of the small intestine of sheep.

The most important nonabsorbable sutures are silk, cotton, nylon, linen, horse-hair, and various metallic wires such as tantalum, stainless steel, and silver. Sutures may be coated or uncoated and may be designated either Type A, *untreated or capillary*, untreated for reduction of capillarity or Type B, *treated or noncapillary*, treated (usually by coating with a wax) to reduce capillarity. If sterilized, nonabsorbable sutures may be impregnated with a suitable bacteriostatic agent or preserved in a suitable packaging fluid.

**Silk** (*q.v.*) is the most widely used nonabsorbable suture at the present time. As ordinary sewing silk, weighed with fillers to lend luster, is impaired both as to strength and elasticity, selected grades of degummed silk fibers are utilized which consist chiefly of the protein fibroin as extruded by the silkworm. The pure silk threads are either twisted or braided to form "twisted silk sutures" or "braided silk sutures." The braided silk is by far the more popular with the surgeon. Most surgeons prefer silk sutures that have been dyed black, this color being more readily perceptible in the wound cavity and tissue.

Most modern surgical silk is so treated as to be noncapillary, to prevent the entrance of moisture or bacteria into the interstices of the braided silk.

Sterile silk is generally packaged much as catgut is, in sealed glass tubes, while unsterilized silk is sold on 25-yard and 100-yard spools and in precut lengths in paper envelopes. Nonsterile silk is usually sterilized in the hospital by autoclaving at 121.5°C. for 30 minutes.

Silk sutures are used in a very wide variety of surgical procedures, as in the brain, eye, gastrointestinal tract, nerves, blood vessels, or, in general, in any wound that is not infected. In the presence of infection, the interstices of silk strands protect bacteria from antiseptics and from the body's defense mechanisms, so that chronic sinuses may form which do not heal until the silk is removed or is sloughed out by the tissues.

**Artificial silkworm gut or dermal sutures** consist of natural twisted silk encased in a nonabsorbable coating of tanned gelatin or other protein substance. This coating must withstand autoclaving without stripping, and its purpose is to prevent the ingrowth of tissue cells which would interfere with its removal after use as a skin or dermal suture. This product is marketed sterile in tubes or unsterilized in boxes, and its chief uses are as stay sutures and skin sutures.

**Silkworm gut** is made from the secreted fluid which the worm would normally use to spin into silk. Just before it is ready to spin its cocoon, the silkworm is killed by immersion in a vinegar bath. The silk sac is removed from the worm; the contents, which congeal on contact with air, are stretched by hand to a length of about 18 in. These filaments are dried in the sun and harden quickly. They are then bleached, polished, and sorted into sizes. This provides a strong, smooth, inert, monofilament suture of the same composition as ordinary silk. The strands may be sterilized by autoclaving. They are quite stiff and require additional boiling in water

to soften them sufficiently for use. Silkworm gut is used principally for suturing the skin and as a stay or tension suture. It is marketed as fine, medium, or coarse in sterile or unsterilized form.

**Surgical cotton sutures** are made of twisted rather than braided cotton fiber. They are made from long-staple Egyptian cotton and are prepared without the use of talcum and other irritating fillers found in ordinary sewing cotton. Cotton sutures differ from silk in that the cotton gains about 10% in tensile strength when wet, but cotton is still the weakest of all widely used suture materials.

Cotton shrinks when autoclaved or boiled, so it should never be sterilized on the original tightly wound spools.

**Nylon** is a synthetic polyamide (*q.v.*) plastic of low tissue reactivity which appears to be quite unaffected by tissue fluids. It will not support bacterial growth and has high tensile strength. Flexibility, smoothness of strand surface, and uniformity of strand diameter are other desirable characteristics. It is generally dyed black or green for easy identification in tissue.

Nylon is supplied both as a monofilament strand and as a braided filament suture. A distinct disadvantage of the monofilament nylon is the difficulty in achieving a secure knot. Multifilament braided nylon, however, appears to be similar to braided silk in knot-holding power. Monofilament nylon is used as a skin or stay suture or for plastic surgery. Braided nylon is more often buried in tissues and is subject to the same limitations as braided silk in the presence of infection.

**Linen** is one of the oldest known suture materials but is currently used to only a limited extent. The advantage of linen resides in its high tensile strength and its stability during sterilization. However, it is nonuniform in diameter, and it tends to cause sinuses in the presence of infection. An important modification of linen, produced by coating it with collodion, is known as *Pagenstecher's linen* and is used principally for the purse-string suture at the base of the appendix after an appendectomy. A few surgeons use both forms of linen in general surgery in preference to silk.

**Horsehair sutures** come from the tail and, to a limited extent, from the mane of the horse. They are characterized by fine gage, a flexibility which makes them easy to handle, noncapillarity, and a minimal tissue reaction. They are, however, of varying diameter along the strand and possess relatively low tensile strength. They require thorough sterilization and are used primarily for skin closure and plastic surgery because of the inconspicuous residual scar.

**Metallic Sutures.** Although many varieties of metal wire sutures have been used in the past, tantalum and stainless steel are about the only metal sutures used today.

*Tantalum* (*q.v.*), a bluish gray metal, is favored as a suture because it is biologically inert, nonirritating to body tissues, and possesses high tensile strength. It seems to resist completely all corrosion and chemical attack by body cells and fluids. Its pliability enables fine-gage wires to be tied in tight knots and heavier wires to be easily twisted. Its malleability makes it useful in sheet form, as skull plates and for other prosthetic purposes. An outstanding feature of tantalum is that, when implanted in tissue, fibroblasts adhere to it tenaciously and form a layer of connective tissue about the metal, whether it be plate, wire, or gauze.

Tantalum wire is of chief interest to orthopedic and plastic surgeons. It is frequently used in fastening fine tantalum wire gauze to body tissues where the mesh is

used in the repair of hernias. Tantalum wire, both monofilament and braided, is supplied in a wide range of diameters comparable to silk sutures.

Tantalum gauze, which is supplied in sheets 6 by 12 in., is made from 0.003-in. wire woven 50 x 50 to the inch and is used in the repair of all types of hernias, especially those apt to recur.

Tantalum metal is also supplied in plates 6 by 6 in. of varying thicknesses for use as skull repair plates and other bone replacements.

Sterilization of tantalum surgical products is readily accomplished by autoclaving. In all cases, grease films should be removed by appropriate solvents, such as chloroform, before sterilization.

*Stainless steel* has been used as a wire suture, as a fixation plate for broken bones, and for screws of many sizes and uses. In addition, stainless steel mesh has gained considerable acceptance.

Today the physical properties of some modern stainless steels are generally satisfactory for surgical purposes. However, there are many varieties of stainless steels, and only the proper selection can avoid considerable corrosion of the metal in tissue with the consequent production of pain-producing metallic ions. Stainless steel surgical products are sterilized by autoclaving.

*Silver (q.v.).* Among the older materials which are still used to some extent are silver wire, foil, and hemostasis clips. Silver is alleged to have some antiseptic action, but in many tissues it is definitely irritating. Little investigation or interest has been reported on silver as a suture material in recent years.

### Surgical Needles

Surgical needles are essentially a part of the suture. They fall into two general classifications: *eyed* needles, those that must be threaded with a suture by the surgeon, and *eyeless* (swaged) needles, which come already firmly fastened to one or both ends of the suture and offer great advantage in minimizing trauma. Both eyed and swaged needles come in many sizes, thicknesses, and shapes. The principal shapes are: straight, half-curved, half-circle and  $\frac{3}{4}$  circle.

### Bibliography

- (1) Bullock, W., Lampitt, L. H., and Bushill, J. H., *The Preparation of Catgut for Surgical Use*, His Majesty's Stationery Office, London, 1929.
- (2) Cook, E. F., and Martin, E. W. (eds.), *Remington's Practice of Pharmacy*, 10th ed., Mack Publishing Co., Easton, Pa., 1951, pp. 1267-76.
- (3) Faudre, A., *Le Catgut*, Masson et Cie., Paris, 1944.
- (4) Holder, E. J., *Postgraduate Medical Journal*, **25**, 427 (1949).
- (5) U.S. Pat. 2,637,321 (May 5, 1953), Arthur Cresswell (to American Cyanamid Co.).

A. A. STONEHILL

**SWEET BASIL OIL, SWEET BIRCH OIL.** See *Oils, essential*, Vol. 9, p. 576, 577.

## SWEETENING AGENTS

A wide variety of chemical substances have the power to evoke a sweet taste to a greater or lesser degree. Unlike sour substances, which are acids, and saline substances, which are salts, the sweet-tasting compounds belong to no well-defined chemical class. Lead and beryllium are examples of inorganic ions that are sweet. Among the organic compounds, little success has been achieved in attempting to correlate sweetness with constitution. So-called "glucophore" groups have been pointed out (10) which, under specific circumstances, are associated with sweetness. However, many classes of organic structures contain compounds that are sweet.

The sweetness of substances varies somewhat with concentration, and, in general, is more powerful in dilute solutions than in strong solutions. Table I, drawn principally from Karrer (8), gives approximate sweetness of some organic substances.

TABLE I. Relative Sweetness of Various Organic Substances.

Substance	Formula	Sweetness (sucrose = 1)
Sucrose	$C_{12}H_{22}O_{11}$	1
Lactose	$C_{12}H_{22}O_{11}$	0.27
Dulcitol	$C_6H_{14}O_6$	0.41
Mannitol	$C_6H_{14}O_6$	0.45
Sorbitol	$C_6H_{14}O_6$	0.48
Glycerol	$C_3H_8O_3$	0.48
Ethylene glycol	$C_2H_6O_2$	0.49
D-Glucose	$C_6H_{12}O_6$	0.5-0.6
Maltose	$C_{12}H_{22}O_{11}$	0.6
Invert sugar	—	0.8-0.9
D-Fructose	$C_6H_{12}O_6$	1.0-1.5
p-Anisylurea	$CH_3OC_6H_4NHCONH_2$	18
Sodium cyclohexylsulfamate	$C_6H_{11}NHOSO_3Na$	30
Chloroform	$CHCl_3$	40
5-Methylsaccharin	$CH_3C_6H_3(CO.NH.SO_2)$	200
Dulcin	$C_2H_5OC_6H_4NHCONH_2$	70-350
6-Chlorosaccharin	$ClC_6H_3(CO.NH.SO_2)$	100-350
n-Hexylchloromalonamide	$n-C_6H_{13}CCl(CONH_2)_2$	300
Saccharin	$C_6H_4.CO.NH.SO_2$	200-700
5-Nitro-2-ethoxyaniline	$NH_2C_6H_3(OC_2H_5)NO_2$	950
Perillaldehyde anti-aldoxime (Perillartine)	$CH_2=C(CH_3)C_6H_5CH=NOH$	2000
5-Nitro-2-propoxyaniline (P-4000)	$NH_2C_6H_3(OC_3H_7)NO_2$	4100

In order to be an acceptable sweetener of commercial utility, a substance must have sufficient sweetening power, be nontoxic, and be reasonably inexpensive to use.

The naturally occurring sugars (*q.v.*) are the oldest and most widely used sweetening agents. Sucrose is most commonly used, followed by glucose to a lesser degree. Polyhydric alcohols, such as sorbitol and glycerol, are used to some extent for their sweetening power, but usually this property is only incidental to their main purpose of acting as a humectant and providing texture, body, or other properties. See also *Alcohols, higher polyhydric; Glycerol*.

Nonnutritive sweeteners are useful in those applications where it is desired to avoid the caloric value of the sugars. Since they have no food value, these sweeteners find their principal use as a part of the diet of those people, including diabetics, who should avoid excessive caloric intake. In addition to use in home preparation of low-calorie diets, nonnutritive sweeteners are also used in the manufacture of commercially processed and packaged dietetic foods such as canned fruits, gelatin desserts, carbonated beverages, dietetic candies, jams, jellies, and frozen desserts. Nonnutritive sweeteners are also used for sweetening dentifrices (*q.v.*), mouthwashes, cosmetics (*q.v.*), medicinal preparations, and tobacco (*q.v.*), particularly where the presence of sugar might lead to spoilage by fermentation or mold growth.

Since the discovery in 1879 of saccharin, the earliest of the nonnutritive sweeteners, many substances have been synthesized and evaluated as sweetening agents. Only saccharin and cyclamate (the sodium and calcium salts of cyclohexylsulfamic acid) are both sufficiently sweet and nontoxic to be considered safe nonnutritive sweeteners by the Food and Drug Administration for use as food additives (7). Both saccharin and cyclamate are adaptable to all ordinary methods of food processing and preparations, including cooking, canning, baking, boiling, and preserving.

Both saccharin and cyclamate in excessive concentrations tend to display a bitter note to the taste. The exact concentration at which this effect occurs varies with the individual. With saccharin the threshold occurs in the vicinity of 0.1%. In the case of cyclamate, the bitter note may be encountered by most individuals at a concentration of approximately 0.8%. These concentrations in both instances are well above the level of ordinary use.

There has been much legislation all over the world against the indiscriminate use of nonnutritive sweeteners in food products. At first, prohibitions were based on the grounds of possible harmfulness; however, since the harmlessness of the acceptable nonnutritive sweeteners has now been established, the present federal regulations allow their use in foods in interstate commerce when such foods are properly labeled.

### Saccharin

Saccharin (I), U.S.P. XIV (insoluble saccharin, gluside, *o*-sulfobenzoic imide, *o*-benzosulfimide, benzoic sulfimide, garantose, saccharinal, saccharinose, saccherol, saxin, sykose; 1,2-benzisothiazolin-3-one 1,1-dioxide, 2,3-dihydro-3-oxobenzisulfonazole), formula weight 183.18, occurs as white crystals or a white crystalline powder, m.p. 226–36°C. Saccharin was first synthesized by Ira Remsen and C. Fahlberg, who discovered the sweetness of the compound in the course of an academic investigation at Johns Hopkins University in 1879 on the oxidation of *o*-toluenesulfonamide. It may be used wherever a nonnutritive sweetener is desired.

### PROPERTIES

One gram dissolves at 23°C. in 290 ml. water, 31 ml. alcohol, 12 ml. acetone, about 50 ml. glycerol, and in 25 ml. boiling water; it is freely soluble in solutions of alkali carbonates and slightly soluble in chloroform and ether. In dilute solutions, it is about 500 times sweeter than sucrose. Sixty milligrams is equivalent in sweetening power to about 30 grams of sucrose. Its solutions are acid to litmus.

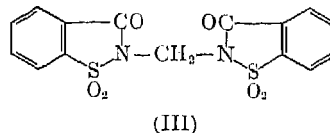
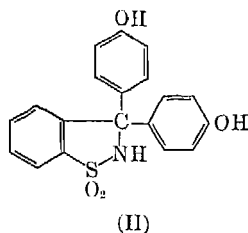
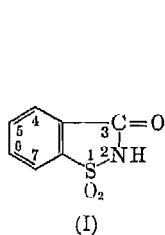
*Saccharin sodium*, U.S.P. XIV,  $C_6H_4CO.NNa.SO_3.2H_2O$ , formula weight 241.21,



after drying at 120°C. for four hours, contains not less than 98% of anhydrous saccharin sodium. One gram is soluble at 23°C. in 1.5 ml. water and about 50 ml. alcohol. When in powdered form, it usually contains about half the theoretical amount of water of hydration due to efflorescence.

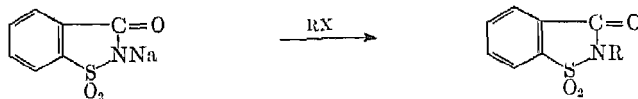
Saccharin is stable under all conditions ordinarily encountered in food preparation and processing, and no loss of sweetening power nor development of off flavors due to instability is encountered. For all practical purposes, saccharin in aqueous buffered solutions of pH 3.3, 7.0, and 8.0 is unaffected by heating at temperatures up to 150°C. for one hour (4).

The structure of saccharin (I) makes many types of reactions possible. The imido hydrogen is acidic, and, therefore, saccharin forms salts with bases. Many metallic salts have been prepared, not all of which are sweet. The copper salt is astringent, and the nickel salt only slightly sweet.



Chlorination of saccharin sodium in water solution yields 2-chlorosaccharin (2).

Saccharin sodium will react with a great variety of halogen compounds to give N-alkyl- or -aryl-substituted saccharin (2):

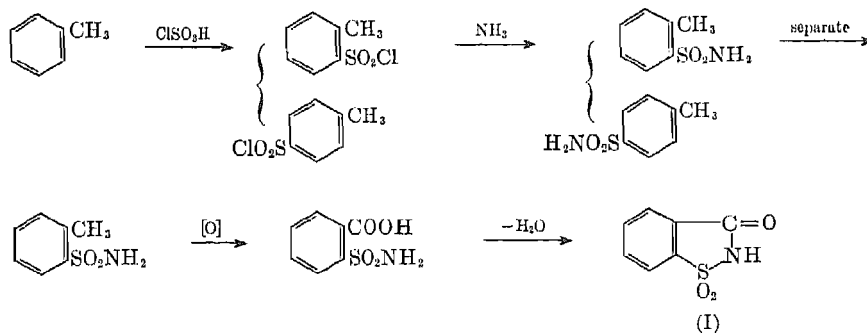


Saccharin condenses with phenols (14) to give *sacchareins* of type (II). Heating saccharin with 40% formaldehyde in sulfuric acid yields 2,2'-methylenebisaccharin (2,2'-methylenebis(1,2-benzisothiazolin-3-one)), (III) (1). The chemistry of saccharin and its derivatives has been investigated by Mameli and Mannesier-Mameli (9).

#### MANUFACTURE

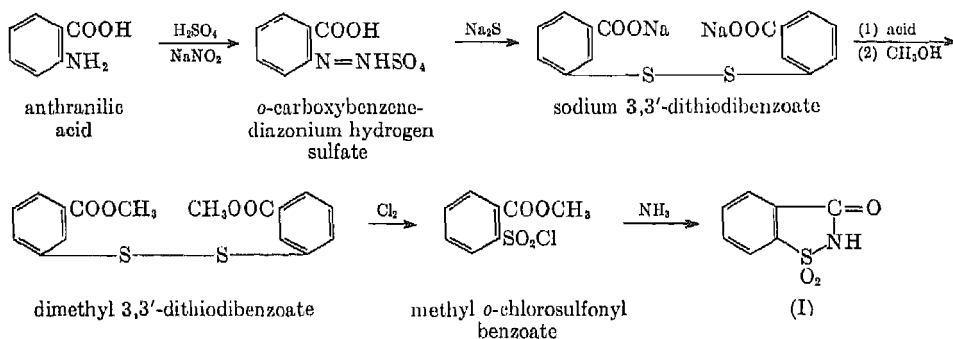
The best-known process for manufacturing saccharin today consists essentially of the same method used by Remsen and Fahlberg in 1879. Toluene and chlorosulfonic acid react at 0-5°C. to form a mixture of *o*- and *p*-toluenesulfonyl chlorides, which is converted by means of ammonia to a mixture of *o*- and *p*-toluenesulfonamides. The mixture is separated, and the *o*-toluenesulfonamide is oxidized to *o*-carboxybenzenesulfonamide (*o*-sulfamoylbenzoic acid). This compound loses a mole of water to become saccharin (I) (see Scheme 1). The *p*-toluenesulfonamide is also an important by-product of saccharin manufacture, and is used as a raw material in the production of chloramine-T (see Vol. 3, p. 670) and sulfonamide plasticizers (see also *Toluenesulfonic acids*).

SCHEME 1



Many modifications of this basic process, particularly of the oxidation step, have been proposed so as to achieve the best possible yields and conversions. Orelup (15) used chromic acid mixed with sulfuric at over 50% concentration, and this is the method most widely used today. Altwegg and Collardeau (14) found the addition of sulfates of iron, chromium, or manganese to be helpful. Löwe (12) used an electrolytic method in which *o*-toluenesulfonamide is suspended in a weak solution of alkali carbonate. This reaction is favored by the presence of lead, cerium, or manganese. Klages (13) used an electrolytic process with addition of permanganate as an oxygen carrier. Alkaline potassium permanganate and alkaline potassium ferricyanide have also been employed. A synthesis of saccharin based on anthranilic acid, which is used commercially in the U.S., is shown in Scheme 2 (3).

SCHEME 2



Numerous other syntheses of saccharin have been devised, and some of these have been used commercially in various parts of the world for one reason or another (5,6).

U.S.P. XIV sets forth specifications for both saccharin and saccharin sodium on melting point, loss on drying, heavy metals, residue on ignition, readily carbonizable substances, benzoic acid and salicylic acid, and assay. Analytical methods are also given.

### Cyclamates

Cyclamate sodium, the first of the cyclamates, was synthesized by Michael Sveda, who discovered its sweetness by accident in the course of experimental work at the

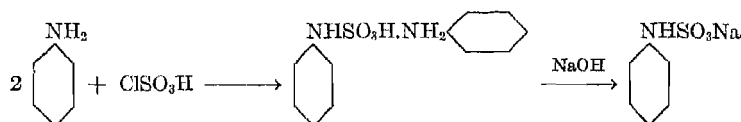
University of Illinois in 1937 (1). Both cyclamate sodium and cyclamate calcium may be used where a nonnutritive sweetener is desired. Both salts are stable under all conditions ordinarily encountered in food preparation and processing, and no loss of sweetening power nor development of off flavors due to instability is encountered.

**Cyclamate sodium**, N.N.R. (sodium cyclohexylsulfamate, Sucaryl Sodium),  $C_6H_{11}NH SO_3Na$ , formula weight 201.23, is a white, crystalline, practically odorless powder with a very sweet taste. It is freely soluble at 23°C. in water and practically insoluble in alcohol, benzene, chloroform, and ether. The pH of a 10% solution is between 5.5 and 7.5. Cyclamate sodium is about 30 times as sweet as sucrose.

**Cyclamate calcium**, N.N.R. (calcium cyclohexylsulfamate dihydrate, Sucaryl Calcium),  $(C_6H_{11}NH SO_3)_2Ca$ , formula weight 432.57, is a white, crystalline, practically odorless powder with a very sweet taste. It is freely soluble at 23°C. in water and practically insoluble in alcohol, benzene, chloroform, and ether. The pH of a 10% solution is between 5.5 and 7.5.

#### MANUFACTURE

Cyclohexylamine is sulfonated by dissolving 148.5 parts by weight in 2240 parts by weight of carbon tetrachloride, cooling the solution to 5°C. and precipitating the cyclohexylammonium salt of cyclohexylsulfamic acid by slowly adding 58.3 parts of chlorosulfonic acid, while maintaining the mixture at about 5°C. This precipitate is filtered off and dissolved in 850 parts by weight of water containing 46.3 parts of sodium hydroxide, and the entire mass is evaporated to dryness. The dry residue is dissolved in a minimum of water and sodium cyclohexylsulfamate recrystallized from the solution by cooling (16).



A modification consists of filtering off the precipitate of cyclohexylammonium salt of cyclohexylsulfamic acid. This is treated in solution with barium hydroxide octahydrate and evaporated to dryness, forming the barium salt of cyclohexylsulfamic acid. The dry mass is dissolved in water, excess barium removed by passing carbon dioxide through the solution and filtering, and barium cyclohexylsulfamate obtained by crystallization. The barium salt is suspended in water and treated with sulfuric acid and barium sulfate filtered off. From the filtrate, cyclohexylsulfamic acid is obtained by crystallization (17), and then further treated to obtain the salts.

The sulfonation of cyclohexylamine may be carried out with a variety of sulfonating agents such as metallic chlorosulfonates, sulfur trioxide, pyridine-sulfur trioxide addition compounds, dioxane-sulfur trioxide addition compounds, and ethyl chlorosulfonate.

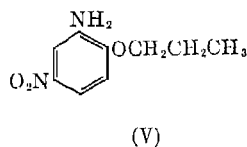
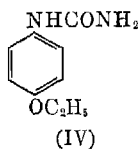
Cyclohexylsulfamic acid can also be prepared by treating cyclohexylamine with sulfamic acid (12a). See *Sulfamic acid*, p. 292.

#### Dulcin

Dulcin (*p*-phenetylurea, sucrol, Valzin) (IV), formula weight 180.20, forms lustrous needles about 250 times as sweet as sucrose. It was first synthesized in 1883 by Berlinerblau. Dulcin is made by treating *p*-phenetidine with phosgene and

then with ammonia. Alternate processes are heating *p*-phenetidine hydrochloride with sodium cyanide and sodium hypochlorite or sodium peroxide in water.

Dulcin is not considered safe for use as a food additive by the Food and Drug Administration (7).



### P-4000

P-4000 (5-nitro-2-propoxyaniline, Verkade's compound) (V) (see Vol. 1, p. 929) is not considered safe for use as a food additive by the Food and Drug Administration (7).

### Bibliography

- (1) Audrieth, L. F., and Sveda, M., *J. Org. Chem.*, **9**, 89 (1944).
- (2) Beilstein, 4th ed., Vol. XXVII, p. 168.
- (2a) Beyer, O., *Handbuch der Saccharin Fabrikation*, Rascher & Co., Zurich.
- (3) *Chem. Eng.*, **61**, No. 7, 128 (1954).
- (4) DeGarmo, O., Ashworth, G., Eaker, C., and Munch, R., *J. Am. Pharm. Assoc., Sci. Ed.*, **41**, No. 1 (1952).
- (5) Dalal, N. B., and Shah, R. C., *Current Sci. (India)*, **18**, 440 (1949); *C.A.*, **44**, 4881c (1950).
- (6) Field Information Agency, Office Tech. Services Rept., **PB-901** (Oct. 10, 1945).
- (7) Fitzhugh, O. G., Nelson, A. A., Frawley, J. P., *J. Am. Pharm. Assoc.*, **40**, No. 11, 583 (1951).
- (8) Karrer, P., *Organic Chemistry*, 4th English Ed., Elsevier, N.Y., 1950, p. 932.
- (9) Mameli, E., and Mannessier-Mameli, A., *Gazz. chim. ital.*, **70**, 855 (1940).
- (10) Moncrieff, R. W., *The Chemical Senses*, Leonard Hill, London, 1951, p. 139.
- (11) Richter, G. H., *Textbook of Organic Chemistry*, Wiley, N.Y., 1938, p. 580.
- (12) Brit. Pat. 174,913 (Jan. 5, 1922), H. Löwe.
- (12a) Brit. Pat. 662,800 (Dec. 12, 1951), Abbott Laboratories.
- (13) Swiss Pat. 78,277 (Nov. 1, 1918), W. A. Klages.
- (14) U.S. Pat. 1,507,565 (Sept. 9, 1924), J. Altwegg and J. Collardeau.
- (15) U.S. Pat. 1,601,505 (Sept. 28, 1926), J. Orelup.
- (16) U.S. Pat. 2,275,125 (March 3, 1942), L. F. Audrieth and M. Sveda (to du Pont).
- (17) U.S. Pat. 2,383,817 (Aug. 28, 1945), J. Robinson (to du Pont).

J. S. RUHOFF

**SWIFT STABILITY TEST.** See *Fats and fatty oils*, Vol. 6, pp. 156-157.

**SYLVANITE**, (Au,Ag)Te<sub>2</sub>. See *Gold*, Vol. 7, p. 276.

**SYLVINITE**,  $x\text{NaCl} \cdot y\text{KCl}$ ; **SYLVITE**, KCl. See *Potassium compounds*, Vol. 11, pp. 13, 15.

**SYMPATHOLYTIC AGENTS; SYMPATHOMIMETIC AGENTS.** See *Cardiovascular agents*, Vol. 3, pp. 219, 220; *Stimulants and depressants of the nervous system*, Vol. 13, p. 18.

**SYNDETS.** See *Surface-active agents*.

**SYNERESIS.** See *Colloids*, Vol. 4, p. 239.

**SYNOL.** See *Oxo and oxyl processes*, Vol. 9, p. 714.

**SYNTANS.** See *Tanning materials*.

**SYNTHESIS GAS.** See *Fuels, synthetic liquid*, Vol. 6, p. 965; *Hydrocarbons*, Vol. 7, p. 638; *Manufactured gas*, Vol. 8, p. 778; *Methanol*, Vol. 9, p. 46; *Oxo and oxyl processes*, Vol. 9, p. 702.

**SYNTHETIC ESTROGENS.** See *Hormones*, Vol. 7, p. 536.

**SYNTHINE PROCESS.** See *Fuels, synthetic liquid*, Vol. 6, p. 960.

**SYNTHOL PROCESS.** See *Fuels, synthetic liquid*, Vol. 6, p. 960; *Oxo and oxyl processes*, Vol. 9, pp. 713, 714.

**SYNTROPAN**,  $\text{C}_6\text{H}_5\text{CH}(\text{CH}_2\text{OH})\text{COOCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{N}(\text{C}_2\text{H}_5)_2 \cdot \text{H}_3\text{PO}_4$ . See *Antispasmodics*, Vol. 2, p. 106.

# T

**TABLETS.** See *Pharmaceuticals*, Vol. 10, p. 237.

**TACAMAHAC.** See *Resins, natural*, Vol. 11, p. 679.

**TACK, TACKINESS.** See *Rubber compounding*, Vol. 11, p. 939.

**TACKIFIERS.** See *Adhesives*, Vol. 1, pp. 200, 202; *Rubber compounding*.

**TACONITE.** See *Iron*, Vol. 8, p. 23.

**TAGETONE, C<sub>10</sub>H<sub>18</sub>O.** See *Terpenes (mono-, acyclic)*.

## TALC

Talc is a natural mineral with the formula, when theoretically pure,  $\text{H}_2\text{Mg}_3(\text{SiO}_3)_4$  or  $3\text{MgO} \cdot 4\text{SiO}_2 \cdot \text{H}_2\text{O}$ . This formula calls for 31.7% MgO, 63.5% SiO<sub>2</sub>, and 4.8% H<sub>2</sub>O. Actually this theoretical composition is very rarely, if ever, found in nature. In apparently "pure" talcs the water content may vary from 3.5 to over 7% with corresponding differences in MgO and SiO<sub>2</sub>. Talc itself generally contains a small percentage of FeO. Materials sold commercially as talcs vary widely from mineralogically "pure" talc. In different deposits or even in different areas in a single deposit, industrial talcs are usually mixed with varying and sometimes large percentages of such accessory minerals as tremolite, serpentine, anthophyllite, magnesite, dolomite, calcite, diopside, chlorite, and quartz. In preparation for market usually no attempt is made to remove these minerals. In fact, some of the important uses for industrial talcs depend on their content of certain accessory minerals. In addition, some talc deposits contain minor amounts of deleterious impurities such as pyrite, iron, and manganese oxides which may make a deposit worthless.

Talc is a metamorphic mineral formed by the alteration of dolomitic limestones and ultrabasic igneous rocks, such as peridotite. In the process of alteration, both talc and serpentine or serpentine alone may have been formed with later alteration of the serpentine to talc. In some cases, talc has been found to be a metamorphic product of magnesia-free minerals and rocks, formed through alteration by hydrothermal action of magnesia-bearing waters.

*Soapstone* is a massive rock of which the chief component is talc. Actually many rocks of very variable composition have been called soapstone if they have a soapy or greasy "feel." The talc content may be as low as 50%. Chlorite mica, often present in large amounts, contributes to the softness and soapy "feel," and helps to impart the greenish-gray color often characteristic of soapstone. *Massive talc* has sometimes erroneously been called soapstone. Massive soapstone has been used for laboratory table tops, acid-resistant refractories, stove linings, and foot warmers.

The term *steatite* has had a variety of meanings. It has been used as a synonym for talc, as an alternative name for soapstone, and as a name for any massive talc. Today, the term is used to describe a massive talc of random crystal orientation used for making high-grade electrical insulators and steatite ceramics for technical applications.

*Pyrophyllite*, the hydrous aluminum silicate,  $H_2Al_2(SiO_3)_4$ ,  $Al_2O_3 \cdot 4SiO_2 \cdot H_2O$ , or  $Al_2Si_4O_{10}(OH)_2$ , is sometimes confused with talc, chiefly for the following reasons: the powdered mineral somewhat resembles ground talc in appearance and feel; talc and pyrophyllite compete in some uses; and the U.S. Bureau of Mines combines talc and pyrophyllite production statistics.

Pyrophyllite is a mineral frequently substituted for talc for some uses because it is almost as soft as talc, but considerably cheaper. In 1952, the average price per short ton of pyrophyllite was \$12.85, whereas talc was \$20.80 per short ton. In the same year production of pyrophyllite in the U.S. amounted to 124,487 short tons.

### Properties

The crystal habit of talc is monoclinic, pseudohexagonal. Talc forms needles or plates with rhombic or hexagonal outlines. Macroscopic size single crystals are unknown. Talc occurs in foliated, fibrous, massive, granular, and micaceous forms—rarely in radical aggregates. Fibrous forms may be pseudomorphic after such fibrous or platy minerals as tremolite.

The color of talc may vary from white, greenish white, or light green to brown. Dendritic stains are sometimes found on talc surfaces, especially on massive steatite-type tales. The pure variety has a soft, "greasy" feel and is translucent in thin sections. Its most important property is its softness. The mineral talc is 1 (softest) on the Mohs mineral hardness scale, but apparent hardness of commercial talc is often much higher due to the presence of harder accessory minerals. See *Hardness*.

The index of refraction of talc is 1.54–1.59, specific gravity 2.7–2.8. The microscopic monoclinic crystals show perfect basal {001} cleavage and are somewhat flexible but not elastic. The melting point is about 1530°C., but varies, depending on the purity of the mineral.

Upon heating, talc begins to lose water at 380–500°C., and at 800–840°C. all the combined water of crystallization is lost. Within this temperature range the structure of the talc crystal is destroyed and a new modification of magnesium metasilicate and amorphous silica is formed. At 1200°C. amorphous silica is transformed into cristobalite. Above 1300°C. both clinoenstatite ( $MgO \cdot SiO_2$ ) and cristobalite ( $SiO_2$ ) are present. See *Silica and silicates (mineral)*. An unstable modification, protoenstatite, has been found to appear during heating of talc; this modification may spontaneously change to clinoenstatite, the stable modification. These thermal changes are of importance where talc is subjected to high temperatures or used as raw material in ceramics.

Pure talc is not attacked by acids at room temperature. It shows slightly alkaline reaction in contact with water.

### Occurrence

Talc occurs in practically all parts of the world, but only in certain locations in sufficiently large quantities and purity to be of commercial interest. Among foreign sources, France and Italy are the most important suppliers of talc for toilet preparations because their tales excel in softness, color, and freedom from impurities. Canada is an important producer of industrial tales. For carving and machining purposes, Indian, Chinese, and Italian tales have been used. The U.S., however, ranks first in the mine production of talc.

Talc mines in the eastern U.S. are located chiefly along the line of the Appalachian Mountains from Vermont to Georgia. St. Lawrence County of New York State is the largest producer of talc; there talc occurs in the form of beds of schist interstratified with limestones and associated with tremolite. Vermont has been a large talc producer, chiefly from deposits near Johnson, Waterbury, Chester, and Windham. Large deposits of soapstone occur in Virginia, in sheets 100 ft. or more in thickness. It is mined in blocks and cut into tabletops and machined into various forms for chemically resistant equipment.

San Bernardino and Inyo countries of California rank second in talc production. In recent years, large talc deposits have been opened in Montana, and these promise to become reliable sources of steatite type talc.

### Mining and Preparation

Talc is mined both at the surface and underground, but the best grades come from deposits several hundred feet below the surface. In many instances the purity of the final product depends on careful selection of the lump rock before grinding. Modern froth flotation milling methods have been developed for the beneficiation of talc, but this process has been applied commercially only at a single operation in Vermont.

Producers grind most of the talc before it enters the trade, although some consumers buy crude material and grind it to desired specifications in their own mills. Some producers sell crude material to grinders. Practically all talc is ground dry, either in pebble or roller mills. See *Size reduction*. Air-floated material is supplied in particle sizes ranging from minus 100 mesh to 99.9% minus 325 mesh. Still finer products, in the low micron ranges, are made in fluid energy grinding mills. Superfine sizes are supplied which contain average particles as small as 0.8 micron. The large surface area of superfinely ground or micronized talc is of interest to all industries that use talc as filler, lubricant, or absorbent.

Talc nuggets for machining are hand-picked and selected for freedom of cracks and impurities and, therefore, demand premium prices.

In working with talc that may contain tremolite or free quartz, dust conditions should be avoided owing to the possibility of leading to pulmonary fibrosis (see Vol. 5, p. 313). However, talcs that are free from these constituents have been handled for many years without harmful effects.

### Specifications and Standards

Military Specifications MIL-15173 and A.S.T.M. Specification D-605-53-T have been established for talc used in paint. Oil absorption, CO<sub>2</sub> content and fineness of grind are specified. USP XIV talc has limits on lead and arsenic content, also solubility in acids. Depending on its use, various properties are often controlled and specified by mutual agreement between supplier and purchaser. Particle size is usually specified as a percentage passing certain mesh sizes, or for more exacting applications as per cent in various micron ranges. Light reflection is an important specification for talc in paints. Good talc should have a reflectivity of 87-95%. Oil absorption may vary from 16 to 74 lb. of oil per 100 lb. of talc powder. For ceramic uses, lime content must be closely controlled. It may be up to 7% in porous and semivitreous ware, but very low for steatite-type talc.



Practical limits for steatite-type talc have been established as follows:

SiO <sub>2</sub> .....	Above	59%
MgO.....	Above	30%
Al <sub>2</sub> O <sub>3</sub> .....	Less than	2.5%
CaO.....	Less than	1%
Fe <sub>2</sub> O <sub>3</sub> .....	Less than	1%
Na <sub>2</sub> O + K <sub>2</sub> O.....	Less than	0.4%
Loss on ignition.....	Less than	6%
Soluble lime.....	Less than	1%

Recently, thermal analysis (*q.v.*) has been used successfully as a medium of quality control of steatite-type talc.

### Economic Aspects

In 1952, the total estimated world production of talc, ground soapstone, and pyrophyllite was 1,475,000 metric tons, of which the U.S. produced 37%, followed by Japan with 21.5%. The next largest producers were France, Italy, Norway, Austria, and Spain, in the order listed. Together they made up 21% of the world production. China, Rumania, and the U.S.S.R. have valuable talc deposits, and their output is included in the above estimated world production figure.

In the U.S., New York, California, and Vermont, rank first, second, and third, respectively, in production and sales of talc in 1952. However, if pyrophyllite is included, North Carolina becomes third and Vermont fourth. Table I shows the production in the U.S., by states, in 1952, of talc, pyrophyllite, and ground soapstone.

TABLE I. Talc, Pyrophyllite, and Ground Soapstone Sold by Producers in the U.S. in 1952.

State	Sales, short tons	Value, \$
California	120,574	2,868,255
Georgia	56,491	653,144
Maryland and Virginia	37,755 <sup>a</sup>	356,274
New York	149,837	4,069,771
North Carolina	115,481 <sup>b</sup>	1,771,518
Texas	17,800	216,569
Vermont	71,027	926,646
Other states <sup>c</sup>	24,182	485,140
<i>Total</i>	<i>593,147</i>	<i>11,347,317</i>

<sup>a</sup> Chiefly or wholly ground soapstone.

<sup>b</sup> Chiefly pyrophyllite.

<sup>c</sup> Includes Montana, Nevada (1952), Texas (1950-51), and Washington.

Prices on New York talcs range from \$24.50 for ceramic grades to \$36 or more per ton for micronized paint grades. The price of powered Vermont talc, sold in bags, ranges from \$14.00-17.50 per ton; that of Canadian talc from \$15.00-35.00 per ton. Steatite-grade California and Montana talc, ground minus 200 mesh, is quoted as \$35.00-45.00 per ton; cosmetic and micronized paint grades may be priced up to \$60 or more per ton. Machinable talc nuggets may sell as high as \$100.00 per ton.

### Uses

Any picture of talc production distributed into uses is subject to serious misinterpretation unless the type and source of talc are known. For example, Vermont talcs

are almost completely different from New York tremolitic talcs so that their competition with each other is negligible. Similarly, California and Montana steatite-type talcs have no competition from New York or Vermont talcs. Bureau of Mines *Minerals Yearbook* end-use tables further confound the picture by combining all talcs with ground soapstone and pyrophyllite. From published statistics there is no way to solve the problem, but in Table II compiled from U.S. Bureau of Mines *Yearbook* figures an attempt is made to indicate end-use patterns.

TABLE II. Sales of Talc, Pyrophyllite, and Ground Soapstone 1949-1951.

Use	Sales, tons	% of total	Principal products used
Paint	100,000-145,000	14-23	Chiefly N.Y. and Calif. and Vt. talc
Ceramics	94,700-170,000	20-27	N.Y. and Calif. talc N.C. pyrophyllite (large)
Rubber	53,400- 75,900	11-12	Vt. and Ga. talc, ground soapstone, some pyrophyllite
Insecticides	61,100- 90,400	10-13	All sources
Roofing	44,200- 64,800	9-10	Vt. and Ga. talc
Paper	25,300- 29,600	5	Calif. and some N.Y. and Vt. talc
Toilet preparations	8,400- 11,700	1-2	Calif. talc
All other	74,700- 86,000	12-16	—
<i>Total</i>	461,900-636,000		

In the years 1949-1951, pyrophyllite sales rose from about 100,000 tons to about 120,000 tons or 18-21.5% of the mixed totals noted above. A large part of this production was used in ceramics, chiefly in wall tile. Since practically no pyrophyllite is used in paint and a large tonnage is used in ceramics, it is probably true that the largest single use for talc itself is in paint, despite the figures in the above table.

Since industrial talcs vary so greatly in mineralogical composition and physical structure, the subject of physical and chemical properties of *talcs in general* cannot be covered briefly. Talcs vary in grain shape, grain size, color, chemical composition, sheen, slip, hardness, and other properties. Talcs used for rubber, cosmetics, steatite, paint, and ceramics all differ widely in properties and prices. Thus, for any specific end use, talcs must be chosen which are naturally adapted to such use.

As inert extenders in paint, New York and California talcs compete chiefly against wollastonite and various types of calcium carbonate fillers, both natural and precipitated. Talc, usually shown in paint formulas as magnesium silicate, imparts many valuable properties to oil- and water-vehicle paints for both inside and outside use. It is not an adulterant and talc is included in many Federal paint specifications.

The advantages of talc in ceramic bodies are various. It is a cheap source of magnesium oxide, which acts as a flux. It gives high thermal shock, high electrical resistance at elevated temperature, and also low dielectric loss, and low power factor. It has a high specific heat and high resistance to acid attack. In low-temperature bodies, it increases thermal expansion, and in both high- and low-temperature bodies it decreases moisture expansion.

In dinnerware bodies, the use of talc involves closer control of raw materials, processing, and kiln treatment than is required for the usual feldspathic mixtures. Talc acts as a flux to reduce the amount of feldspar needed to produce the desired

strength and will materially decrease the moisture expansion of porous bodies, thereby avoiding delayed crazing of the glaze.

Tremolitic (lime-bearing) talc is being used in wall tile bodies. Wall tiles of low moisture expansion and high resistance to delayed crazing can be developed by the use of tremolitic talc, in conjunction with pyrophyllite. The same reasoning applies for the use of talc in art ware bodies.

In the electrical porcelain field, the name "steatite" or "steatite porcelain" designates a series of vitrified ceramic bodies containing 70-90% of talc with the remainder of clay, feldspar, or alkaline-earth oxides. Such bodies have high mechanical strength and low dielectric loss and are therefore widely used as insulation for electronic uses. Steatite ceramics are recognized to be of strategic importance and approved sources of supply manufacture steatite ceramics according to Joint Army-Navy Specifications JAN-I-8 and JAN-I-10. The quality of steatite ceramics is also governed by A.S.T.M. Specification D667-44.

Ceramic kiln furniture and insulation for electric heating appliances are often made with talc as a major ingredient, owing to the ability of the material to give high resistance to thermal shock by its development (by combining with alumina) of cordierite crystals ( $\text{Mg}_2\text{Al}_4\text{Si}_5\text{O}_{18}$ ) in ceramic bodies consisting of mixtures of talc, alumina, and clay.

In small amounts, massive talc is still used for the manufacture of gas burner tips, and special insulators which are made by cutting and machining blocks of steatite. This method permits the production of articles to accurate dimensions, without the use of steel dies.

In prepared roofing, coarse, screened fractions of talc are used for granules and fine powder is used as a dusting agent. In rubber, talc is used chiefly as a dusting agent. In cosmetics, talc is a major ingredient of face powders (see Vol. 4, p. 542) and talcum powders. The largest use for talc was once as a paper filler for which purpose it had superior qualities. Clay has now largely taken the place of talc as a cheap paper filler, but some talc is still used. In insecticides and fungicides, talc, chiefly of the lower, off-color grades, is used as an extender. Many other minor uses, taken together, consume a considerable tonnage of ground talc.

Tailors' "chalk" and steel-workers' crayons are sawed from compact massive talc.

### Bibliography

- (1) Ceramic Materials Issue, *Ceram. Ind.*, **62**, No. 1 (125-26) (1954).
- (2) Dana, J. D., and Hurlbut, C. S., *Manual of Mineralogy*, 16th ed., Wiley, N.Y., 1952.
- (3) Engel, A. E. J., "Talc and Ground Soapstone," in *Industrial Minerals and Rocks*, 2nd ed., Am. Inst. Mining Met. Engrs., 1949, pp. 1018-41.
- (4) Gaskins, W. W., "Historical Background Development on Use of Talc in Ceramic Bodies," *Am. Ceram. Soc. Bull.*, **31**, No. 10, 392-95 (1952).
- (5) Gillingham, W. P., "Grinding Talc to Superfine Size," *Compressed Air Mag.*, **55**, No. 2, 32-37 (1950).
- (6) Kauffman, A. J., Jr., and Dilling, E. D., "Differential Thermal Curves of Certain Hydrous and Anhydrous Minerals, with a description of the Apparatus Used," *Econ. Geol.*, **45**, No. 3, 222-24 (1950).
- (7) Ladoo, R. B., "Talc and Soapstone," *U.S. Bur. Mines, Bull.*, **213** (1923).
- (8) Ladoo, R. B., and Myers, W. M., *Nonmetallic Minerals*, 2nd ed., McGraw-Hill, N.Y., 1951, pp. 531-45.

- (9) *Mineral Raw Materials, Survey of Commerce and Sources in Major Industrial Countries.* (Prepared by U. S. Bureau of Mines.) McGraw-Hill, N.Y., 1937.
- (10) *Minerals Yearbook*, U.S. Bur. Mines, annual edition.
- (11) Spence, H. S., "Talc, Steatite, and Soapstone Phyllosilicates," *Can. Bur. Mines, Bull.* **803** (1940).
- (12) Thurnauer, H., and Rodriguez, A. R., "Notes on the Constitution of Steatite," *J. Am. Ceram. Soc.*, **25**, No. 15, 443-50 (1942).
- (13) Trauffer, W. E., "New Fine-Grinding Method," *Pit and Quarry*, **43**, No. 2, 58-62, 64 (1950).

HANS THURNAUER

**TALCUM POWDER.** See *Cosmetics*, Vol. 4, p. 554.

**D-TALITOL**,  $\text{CH}_2\text{OH}(\text{CHOH})_4\text{CH}_2\text{OH}$ . See *Alcohols, higher polyhydric*, Vol. 1, p. 324.

## TALL OIL

Tall oil is "the natural mixture of rosin acids related to abietic acid and of fatty acids related to oleic acid, together with nonacidic bodies, which is obtained by acidifying the black liquor skimmings of the alkaline paper pulp industry" (A.S.T.M. D804-52). Tall oil is obtained entirely from the black liquor of the sulfate (kraft) process of wood pulp manufacture, using resinous woods such as pine. See *Pulp*.

The name is derived from the Swedish *tallolja* (literally, "pine oil"), and was adopted after the term "liquid rosin" (from the German *flüssige harz*) had been prohibited under the Harrison Naval Stores Act. Pine oil is a different product in the U.S. (chiefly  $\alpha$ -terpineol).

Since it is the cheapest suitable organic material available, tall oil is being used in increasing amounts in applications in which the resin acids present in tall oil are either used or can be tolerated.

### Crude Tall Oil

When free from gross contamination (fiber, trash, etc.), crude tall oil shows in thin layers an orange-red color with green fluorescence. The odor is unpleasant and penetrating. The viscosity is variable, increasing with resin acids content and also with material insoluble in petroleum ether (3). Physical tests commonly employed for vegetable oils do not give clearly defined values at low temperatures. Thus crystallization of resin acids is likely to occur before the sample can be cooled to the pour point. Also the titer test is quite low and not very reproducible. The flash point is usually above 350°F. (10).

The composition follows closely that of the ether extract of the wood used to make the paper pulp and varies with the species. Pines give higher yields with higher content of resin acids than do other conifers (9). In the U.S., southern pines give higher yields with more resin acids than northern pines (7), but in Finland the reverse is true (8). See also below under "Composition of Distilled Tall Oil."

The data in Table I (3), based on some 35 or more references, illustrate the wide variations in properties of crude tall oils from various sources.

"The saponification number is always higher than the acid number partly due to esters of fatty acids with sterols and other higher alcohols. (About half the sterols are esterified.) Also fatty acids containing hydroxy acids usually show an ester number due to lactones or 'estolides' (esters of fatty acids with the hydroxy group of a

TABLE I. Properties of Crude Tall Oils.

Property	Value	
	Minimum	Maximum
Density (at various temperatures)	0.95	1.024
Acid number	107	174
Saponification number	142	185
Iodine number	135	216
Ash, %	0.4	4.62
Moisture, %	0.39	7.2
Material insoluble in petroleum ether, %	0.1	8.5
Fatty acids, %	18	60
Resin acids, %	28	65
Nonacid bodies	5	24
Viscosity (18°C.), centipoises	760	$15 \times 10^6$
Viscosity (100°C.), centistokes	150	1200

fatty acid). Even without hydroxy acids the unsaturated acids can form lactones and estolides by addition of a carboxyl to a  $\text{—C=C—}$ . Such additions are catalyzed by conc.  $\text{H}_2\text{SO}_4$ , as in the formation of  $\gamma$ -stearolactone from oleic acid, or the lactone of dihydroabietic acid. Many such complicated reactions may occur in the preparation and treatment of tall oil and these lead to further complications in refining and conversion to derived products" (3).

### Manufacture and Purification

Details of manufacture and purification of tall oil are generally trade secrets. The first step is, of course, separation of skimmings from the black liquor. When the latter has been partially concentrated in vacuum evaporators, usually to around 22% solids, it is led into a tank proportioned for suitable retention time. Liquor outlet and an overflow launder are arranged to permit the curdy "soap" to rise sufficiently to be scraped over the latter by a skimmer.

This removal of skimmings has become almost universal practice because it improves the recovery of chemicals from the black liquor. Not all skimmings are made into tall oil at the mill. Some mills, especially those of smaller capacity, either sell the skimmings to tall oil producers or burn them in their recovery furnace, depending on market value. After as much black liquor as possible has settled out, a typical composition is: 30–35% water, 5–10% black liquor solids, the remainder being the soap. It has a fuel value of 8000 to 9000 B.t.u. per pound and a sodium content of around 6% as  $\text{Na}_2\text{O}$ . Nomographs have been prepared which correlate the value of skimmings with tall oil yields and costs of salt cake and fuel (11).

The skimmings are acidified, usually with sulfuric acid, although some European kraft mills are reported to use niter cake,  $\text{NaHSO}_4$ . Sulfurous acid appears to remove some of the color and odor; therefore its use might be justified. Operation may be either batch or continuous. For the latter automatic pH control is advantageous. It is important to avoid even slight alkalinity at the end, since otherwise troublesome emulsions may form. These are difficult to break even by reacidifying.

The acid should not be too concentrated lest polymerization of unsaturated compounds be induced or the disparity in volumes make uniform mixing difficult. Commonly 66°Bé. acid is diluted with four volumes of water before use. Lead may be

employed for parts in contact with the acid although acid-proof tile is preferable. Separation of the liberated tall oil is facilitated by heat; therefore the temperature is usually maintained near 100°C. The oil is decanted. A third phase formed between the oil and the acid water contains lignin, fiber, and other contaminants. Still other impurities settle out on standing. If allowed to cool, resin acids will crystallize, and at 25°C. any excess above 35% will thus separate. The liquid portion will then be darker than the whole oil. The resin acid crystals may be purified by recrystallization from a suitable solvent, such as methanol. In this way it is possible to obtain pure resin acid crystals melting at 170–175°C. (capillary method). These can be fused to a clear resin lighter than WX (rosin type), but unless stabilized by disproportionation will recrystallize, evolving heat and darkening in color (6). See also Vol. 11, p. 782.

#### PURIFICATION

Many methods have been suggested for purification of tall oil and for preparation of useful derived products. West (12) lists 32 journal articles and 118 patents on purification out of a total of 1056 literature references on tall oil. The methods most frequently mentioned may be classified as follows:

- (1) Removal of color and odor:
  - (a) Treatment (usually in a solvent) with mineral acid;
  - (b) Adsorption on activated carbon, decolorizing clay, or fuller's earth, the tall oil usually in a solvent.
- (2) Distillation under reduced pressure:
  - (a) Alone;
  - (b) With other gases: steam, inert gases, solvent vapors.
- (3) Partition between immiscible solvents:
  - (a) After partial or complete esterification;
  - (b) After partial neutralization;
  - (c) Without prior treatment, using selective solvents.

One purification method used with more or less modification by a number of refiners involves dissolving the crude tall oil in a neutral solvent, for example, naphtha, stirring with 66°Bé. sulfuric acid at ordinary temperatures (15–25°C.) for about one hour. The acid used amounts to about 7% of the weight of crude. The acid sludge is drawn off or centrifuged, washed with small portions of the solvent, and the washings added to the tall oil solution. This is washed with hot water (for example, by reflux) until free of acid. The solution is then decolorized with bleaching clay or fuller's earth, filtered, and the solvent distilled. A 2-stage acid treatment, with 40% of the acid in the first stage, gives better color. Phytosterol may be recovered from the first sludge (14).

Purification by acid treatment makes no essential change in the composition of tall oil other than removal of some impurities, color, and odor. Subsequent crystallization may reduce the resin acids content, but not below saturation. Distillation can yield fractions differing greatly from the crude. Thus one continuous vacuum distillation is reported to produce (13):

(1) A fatty acid fraction with not more than two per cent of resin acids, low in saturated acids, and with equal amounts of oleic and linoleic; no linolenic. This is useful in nonyellowing alkyls, paste and liquid soaps, emulsifying agents, and for chemical derivatives.

(2) A resin acids fraction containing 70% resin acids similar to those of wood

rosin and 25% fatty acids, mostly linoleic, of which about one-fifth is conjugated. When esterified, as in a maleic-pentaerythritol-resin ester, these fatty acids form 25% of an excellent drying oil which replaces a corresponding amount of oil in the final varnish.

The properties of five commercial American tall oil products are shown in Table II (3).

TABLE II. Properties of Five American Tall Oils.

Sample (trade name)	Purification method	Color (Gardner)	Acid no.	Saponification no.	Iodine no.	Fatty acids, %	Resin acids, %	Unsaponified, %
Unital <sup>a</sup>	Acid precipitation	9-11	155-164	168-169	150-170	43	51	5.6
Facoil <sup>b</sup>	Solvent extraction	10-12	166	174	143	47-51	42-46	7.8 max.
Liqro <sup>c</sup>	Whole tall oil	—	160-170	165-175	190-210	45-50	42-48	6 to 9
Rosoil AH <sup>c</sup>	Single distilled	11-14	155-163	158-166	155-165	37-45	61-66	8-12
Indusoil <sup>c</sup>	Double distilled	9-11	180-183	180-185	170-180	46-52	30-33	4-6

<sup>a</sup> A product of Union Bag & Paper Corp.

<sup>b</sup> National Southern Products Corp.

<sup>c</sup> The others are made by West Virginia Pulp & Paper Co.

Equipment and operating details are trade secrets. At elevated temperatures (530° F. or over) the fatty acids are very corrosive. 18-8 stainless steel will not resist corrosion by these acids, but the addition of 3% molybdenum gives better passivity. The minimum for satisfactory service appears to be 22 Cr-8 Ni.

#### COMPOSITION OF DISTILLED TALL OIL

In addition to separating components, vacuum distillation produces changes in chemical composition, since the tall oil is heated to 250-280°C. (depending on pressure and other factors).

At these temperatures a series of chemical reactions may occur. The phytosterols and other alcohols that have been free in the tall oil are esterified. Part of the sterols may decompose. Part of the fatty acids are polymerized through formation of 6-member carbon rings by diene addition. The abietic type resin acids are further isomerized and disproportionated to dehydro-, dihydro-, and tetrahydroabietic acids, or may be dehydrogenated with evolution of hydrogen. Part of the resin acids decompose to hydrocarbons and carbon dioxide, or carbon monoxide, and water. The carboxyl groups of another part of the resin acids are added to the double bonds of fatty acids, or of other resin acids, to give estolides. Some resin acids may split off water to form anhydrides. The final result is that the distillation products of tall oil may contain small amounts of compounds not in the starting material.

"Except for some separation of palmitic and more volatile acids in the first fraction the fatty acids of tall oil distillates have nearly the same composition as in the crude tall oil, i.e., they will normally consist of almost equal parts of oleic and linoleic (including isomerized, i.e., conjugated, linoleic) acids with a linolenic content less than 1%. Small amounts of adipic,  $\text{HOCO}(\text{CH}_2)_4\text{COOH}$ , and sebacic,  $\text{HOCO}(\text{CH}_2)_8\text{COOH}$  acids have been found in distilled tall oil. They are formed by decomposition of oleic and other fatty acids. No data have been published on the composition of the rosin acids in the fatty acid fraction. It can be assumed the dextropimaric type will be con-

centrated in the fatty acid fraction since these rosin acids are more volatile than the rest. The presence of these rosin acids as lactones in the fatty acid fraction might help explain the difference between the saponification number and the acid number. Since most of the alcohols in crude tall oil are believed to be esterified during distillation the unsaponifiables in the fatty acids fraction must consist chiefly of hydrocarbons. The distilled fatty acids do not contain any material insoluble in petroleum ether" (3).

Eight resin acids, all of which may occur in tall oil have been studied (see *Rosin*) five of which have the empirical formula  $C_{20}H_{30}O_2$ . The acids are of two types, the abietic type (abietic, levopimaric, neobietic, dehydro-, dihydro-, and tetrahydro-abietic acids) and the pimaric type (dextro- and isodextropimaric acids). The latter can be obtained from a mixture of resin acids by distillation; therefore it seems probable they would be concentrated among the resin acids in distilled tall oil fatty acids.

Hibbert and Phillips have stated the following: the nonacidic bodies of tall oil consist mainly of alcohols and hydrocarbons. Only a few of these have been identified: the main component (70-90%) appears to be  $\beta$ -sitosterol,  $C_{28}H_{48}O$ , m.p. 136-37°C. A sterol with rotation  $[\alpha]_D + 24.8^\circ$  has been reported also. The latter appears in greater abundance in the "tall oil pitch." Therefore it is thought to be formed by hydrogenation of  $\beta$ -sitosterol during the distillation. Some lignoceryl alcohol,  $C_{24}H_{48}OH$ , m.p. 76°C., has been found also. It is presumed identical with the "wax" reported in the unsaponifiable portion of the ether extract from jack pine (3,6).

### Economic Aspects

Although commercially available in Europe before 1920, tall oil was not produced extensively in the U.S. until the mid-1930's. Most recent data for production are (in thousands of pounds):

<u>Year</u>	<u>Crude</u>	<u>Refined</u>
1950 (1)	309,802	112,013
1951 (1)	398,237	134,580
1952 (2)	312,770	102,860
1953 (2a)	318,453	118,765

Throughout 1952 and 1953, crude tall oil sold at between \$40 and \$45 per ton and the refined or distilled tall oil sold between \$100 and \$150 per ton depending on its quality.

Recent and continuing expansion in alkaline pulping of resinous woods, especially in the southern U.S., has already raised the potential production of tall oil above 1000 tons per day. Attainment of this rate depends on economic conditions. During peacetime, tall oil competes with imported vegetable oils and raw materials like copra as well as with domestic production of cottonseed, linseed, soybean, tung, and similar vegetable oils. In the time of war cessation of imports will create a shortage which tall oil can supply. A small increase in market value can bring into production virtually all of the easily recoverable skimmings. Because tall oil is a product of the stable and expanding alkaline paper pulp industry, the market price is not subject to fluctuations due to seasons, crop failures, transportation difficulties, etc. (10).



### Uses

Uses for tall oil and its derivatives include the preparation of adhesives, asphalt emulsions, binders, coil oils, detergents, driers (*q.v.*), drying oils, emulsifiers, flotation agents, greases, linoleum, penetrating oils, printing inks, resins, rubber chemicals, soaps, textile oils, varnishes, and wetting agents.

One of the most important and rapidly growing uses of tall oil is in the preparation of esters for use in drying oils; additives for lubricants, for example, extreme-pressure greases and cutting oils; hydraulic fluids; surfactants such as wetting agents, and emulsifying and demulsifying agents; plasticizers; and resins. Also together with phthalic or maleic acids and polyhydric alcohols, especially pentaerythritols, tall oil esters form alkyd resins of superior weather-resistant properties.

### Bibliography

- (1) *Annual Survey of Manufactures* (3rd) for 1951, U.S. Dept. of Commerce, p. 195.
- (2) Bureau of the Census, *Facts for Industry*, Series No. M17-1-02.
- (2a) Bureau of the Census, *Facts for Industry*, "Animal and Vegetable Fats and Oils, 1953."
- (3) Gabrielson, C. O., *Iva*, **21**, No. 4, 162-84 (1950). (17 tables, 2 figures, 106 references.)
- (4) Göther, I., *Svensk Papperstidn.*, **45**, No. 9, 169-173 (1942).
- (5) Hasselstrom, T., Brennan, E., and Hopkins, S., Jr., *J. Am. Chem. Soc.*, **63**, 1759-60 (1941).
- (6) Hibbert, H., and Phillips, S. B., *Can. J. Research*, **4**, 1-34 (1931).
- (7) Jennings, W. H., *Paper Trade J.*, **126**, No. 9, 137-38, Tappi Sect. 134-135 (1948).
- (8) Juvonen, V. V., *Suomen Kemistehtiä*, **A20**, 18-28 (1947).
- (9) Nichols, R. V. V., *Chemistry in Canada*, **38**, 122 (June 1953).
- (10) Pollak, A., *Tall Oil in Industry* (Bull. No. 3), The Tall Oil Assoc., N.Y.
- (11) Pollak, A., and Wiley, Paul R., *Paper Trade J.*, **125**, No. 9, 37-40 (1947).
- (12) West, Clarence J., *A Bibliography of Tall Oil*. The Institute of Paper Chemistry, Appleton, Wis. (1947-50, continuing).
- (13) Wheeler, D. N., Foster, R. J., and Berry, A. P., *Am. Paint J.*, **37**, No. 24, 62-66 (1953).
- (14) U.S. Pat. 2,223,850 (Dec. 3, 1940), Frederick H. Gayer and Charles E. Fawkes (to Continental Research Corp.)
- (15) U.S. Pat. 2,396,651 (March 19, 1946), Torsten Hasselstrom.

R. H. STEVENS

**TALLOW.** See *Fats and fatty oils*, Vol. **6**, pp. 144, 148, 169; *Meat and meat products*, Vol. **8**, p. 838.

**D-TALONIC ACID**,  $\text{CH}_2\text{OH}(\text{CHOH})_4\text{COOH}$ . See *Sugars (derivatives)*, Vol. **13**, p. 208.

**TANKAGE.** See *Fertilizers*, Vol. **6**, p. 392; *Feeds, animal*, Vol. **6**, p. 308.

**TANK CARS.** See *Packaging*, Vol. **9**, p. 755.

**TANNIC ACID.** See *Astringents*, Vol. **2**, p. 205; *Tanning materials*.

## TANNING MATERIALS

Vegetable tanning materials.....	p. 578
Vegetable tanning materials—chemistry.....	p. 586
Synthetic tanning materials.....	p. 592

For the operations of tanning see *Leather and tanning*. For inorganic tanning materials see such articles as *Chromium compounds*.

## VEGETABLE TANNING MATERIALS

Tanning is the art of processing raw hides or skins into leather by means of a substance called a tan or a substance containing a tanning agent capable of bringing about a tanning effect. In early French and English literature the word tan was used to denote the crushed bark of the oak itself, whereas it is the astringent or tanning principle contained in the bark that is the active tanning or leathermaking agent. The term tanning principle or "principe tannant" was first used by Proust, about the year 1798. At the present time, the tanning principle or agent contained in the barks, woods, fruits, leaves, and roots of a large number of plants and trees is known as tannin. According to Julia de Fontenelle (1790–1842), the first to suggest and use the word tannin was Pelouze, about the year 1834. The purest form of tannin, gallotannic acid, obtained from nutgalls was described by Pelouze as "a colorless, inodorous, very astringent, and water-soluble substance possessing the property of combining with the gelatine of hide substance and converting it into leather."

The tannins are a large group of water-soluble, complex organic compounds, widely distributed throughout the vegetable kingdom. Almost every tree or shrub that grows contains some tannin, in the leaves, twigs, bark, wood, or fruit. The materials commercially used are those which contain a large amount of tannin. Much less than 10% of tannin cannot be economically extracted, particularly from those materials which are of value for their tannin alone. Extraction of tannin from chestnut wood, which contains 5–8%, is largely economical because the spent wood is valuable for papermaking.

Table I gives a classification of a number of the most commonly used vegetable tanning materials in the U.S. Throughout the world there are at least three hundred varieties of tannin-bearing plants and trees.

TABLE I. Principal Sources of Tannin.

Barks	Woods	Fruits	Leaves	Roots
Wattle	Quebracho	Myrobalans	Sumac	Canaigre
Mangrove	Chestnut	Valonia	Gambier	Palmetto
Oak	Oak	Divi-divi		
Eucalyptus	Urunday	Tara		
Hemlock		AlgarroBILLA		
Pine				
Larch				
Willow				

Table II gives some analytical data pertaining to the principal constituents of several varieties of tannin-bearing wood. As a general rule, the water-soluble extract contains about 95% of the total tannin.

TABLE II. Proximate Analyses of Wood.

Wood	Cellulose	Water extract	Resin	Other noncellulose
Oak	45.43	14.04	1.47	39.06
Birch	63.42	3.03	1.30	32.25
Chestnut	57.85	10.14	1.25	30.76
Poplar	71.41	3.27	1.56	23.76
Quebracho	36.78	27.21	1.12	34.89

Table III gives analyses of the water extracts obtained from several of the most commonly used raw tanning materials. The extractions and analyses were made in accordance with the Official Methods of the American Leather Chemists' Association.

TABLE III. Comparative Tannin Analyses.

Constituent	Chestnut wood	Oak bark	Hemlock bark	Quebracho wood	Mangrove bark
Total solids	14.45	24.24	20.84	28.63	44.00
Soluble solids	13.08	21.77	16.76	23.77	37.28
Insolubles	1.37	2.47	4.08	4.86	6.72
Nontannin	5.31	9.28	6.59	3.12	8.78
Tannin	7.77	12.51	10.17	20.65	28.51

Although the natural tannins may differ greatly in chemical constitution and reactions, all have the common property of precipitating gelatin from solution and of combining with collagen and other protein matter contained in hide substance to form leather. In addition, they are precipitated by many organic bases, such as quinine, morphine, and most of the basic coloring matters.

All natural tannins dissolve in water to give solutions that range in color from light straw to dark red and brown, thus indicating that each tannin contains its own characteristic coloring matter. Besides producing leather of a distinctive color, each vegetable tannin produces leather having definite physical and chemical properties that differentiate it from all others. Furthermore, when raw vegetable tanning materials are extracted according to the usual laboratory or plant methods, the liquors differ in pH value from 2.8 for myrobalans to 4.75 for mangrove bark cutch.

The color of each tannin solution, as well as the color it imparts to leather, may be lightened or darkened by lowering or raising the pH value. On increasing the pH, they invariably form compounds that oxidize and darken rapidly, becoming successively orange, brown, and black. In regard to their color value and reactions, the tannins are, for all practical purposes, identical with the natural vegetable dyes generally called dyewoods.

The color reactions of the tannins are of great importance in their identification and classification, and the tannins have been conventionally divided into two principal classes—the catechol tannins and the pyrogallol tannins. Upon dry distillation, the catechol tannins yield catechol as one of the principal products of decomposition, and their solutions give a greenish-black precipitate with ferric salts; the pyrogallol tannins upon dry distillation yield pyrogallol, and their water solutions give bluish-black precipitates with ferric salts. As a general rule, in catechol tannins, only pyrocatechol derivatives are found while in the pyrogallol tannins gallic acid is always present.

The preliminary classification of the common vegetable tanning materials (given in Table IV) is based largely upon the data in (4).

TABLE IV. Classification of Vegetable Tannins.

*Class I. Catechol Tannins*

Bromine water gives a precipitate.  
Iron alum gives greenish black precipitate

Copper Sulfate Followed by Ammonia in Excess

*Class A*  
(Precipitate dissolves)

*Class B*  
(Precipitate insoluble)

Cutch (acacia catechu)  
Quebracho  
Hemlock  
Larch  
Gambier  
Quercitron

Cutch (Mangrove)  
  
Willow  
  
Oak

*Class II. Mixed Tannins*

Bromine water gives a precipitate.  
Iron alum gives blue or purplish blacks.  
Wattle bark  
English oak bark  
Chestnut oak bark  
Babool bark

*Class III. Pyrogallol Tannins*

Bromine water gives no precipitate.  
Iron alum gives blue-black precipitate.

Gallnuts  
Sumac

Myrobalans  
Chestnut

Valonia  
Divi-divi

AlgarroBILLA

Extraction of the tannin from the common raw materials by means of water is comparatively simple. All vegetable tannins are susceptible to destruction by heat; and thus each tanning material has an optimum extraction temperature, given in Table V.

TABLE V. Extraction Temperatures.

Tanning material	Optimum extraction temp., °F.	Tanning material	Optimum extraction temp., °F.
Oak bark.....	195	Sumac leaves.....	140
Myrobalan nuts.....	195	Wattle bark.....	165
Valonia acorns.....	140	Quebracho wood.....	195

The rate at which the tannin can be extracted from any given tanning material depends upon a number of factors of which the most important are the volume and the temperature of the extraction water and the length of time the material is under ex-

traction. The duration of heat is of great importance; for example, often there is less loss of tannin when the raw material is exposed for a short time to temperatures above the theoretical optimum than there is when the material is exposed for too long a time at the optimum temperature or at even lower temperatures.

The leaching or extracting may be carried out either in large open vessels or in autoclaves. In the former method the material is under extraction for several days, while in the latter the material is under extraction only a few hours. In open leaching the temperature of the extraction water rarely exceeds 210°F., while in autoclaves under pressure the temperature may range from 220 to 290°F., depending upon the material being extracted. From this it may readily be seen that the economical extraction of tannin involves the maintenance of uniform conditions of time, temperature, circulation, and the volume of water.

Since the most important use for the tannins is in leathermaking, the ultimate value depends upon the yield of leather obtained, expressed in pounds or square feet. The yield depends upon the stability of the tanning liquors and the tannin-combining or fixation value. The stability of tanning liquors may be measured in terms of their susceptibility to loss of tannin, while in use, by oxidation and fermentation. All vegetable tannins are susceptible to fermentation, which destroys the tannin and leads to the formation of acids, and usually of sugars. Table VI (5) gives some data showing the loss or destruction of tanning that usually takes place upon exposure to air.

TABLE VI. Relationship of Loss of Tannin by Fermentation and Sugar Content of Various Tanning Materials.

Source	Loss of tannin, %	Sugar formed, lb. per 100 lb. tannin
Mangrove bark	0.48	1.3
Wattle bark	2.91	3.2
Valonia acorns	27.51	9.5
Myrobalan nuts	60.24	17.4
Quebracho wood	6.15	1.0
Hemlock bark	14.88	5.8
Chestnut wood	17.00	2.9
Oak bark	21.44	25.2

The most important properties of vegetable tanning materials are the extent to which they combine with hide substance, which is called the *tannin fixation value* or *leathermaking value*, and the rate at which this combination takes place. Table VII gives comparative data, obtained under standard conditions, for three of the materials used for sole leather or heavy leather.

TABLE VII. Fixation of Tannin.

Material	Tannin fixed, lb. by 100 lb. hide protein	Time for penetration, days
Quebracho	28.55	22
Chestnut	44.24	26
Cutch (mangrove)	49.68	30

Those tannins that penetrate the hide slowly usually have the highest fixation or leathermaking value. Tannins with higher fixation are used for heavy leathers, which

are usually sold by the pound. Those having lower fixation values invariably produce thin, soft leather, which is sold by the foot.

Tanners purchase vegetable tanning materials in the *raw state* or in the form of *extracts*. The extracts are shipped in the *liquid*, *solid*, or *powdered* state. In the case of quebracho, the liquid extract is shipped in barrels containing 500 lb., or in tank cars containing 8,000 gal. or 80,000 lb.; the tannin content is 35%. The solid extract is packaged in sacks in the form of cakes weighing 100 lb. and containing 65% tannin. The powder is shipped in bags weighing 100 lb. and containing 80% tannin.

Vegetable tanning materials are bought and sold on a definite tannin percentage basis or on a guaranteed tannin content. When they are sold on a tannin basis, the seller must make full allowance for any deficiency of tannin and, likewise, the buyer must pay for any excess. When they are sold on a guaranteed tannin basis, the buyer is not expected to pay for any excess tannin, but the seller must make due allowance for any deficiency.

The relative values of vegetable tanning materials are generally expressed as *tan unit cost*, that is the cost, expressed in cents, of one pound of tannin. For example, a tanning material sold at 5 cents per pound, on the basis of 50% tannin, would have a tan unit cost of 10 cents. In arriving at the exact cost of any given tanning material, besides the initial tan unit cost, the tanner must take into consideration the ultimate tan unit cost based upon the loss of tannin by fermentation in the tanning liquors, as well as the amount of tannin fixed or permanently combined with the hide. Table VIII gives tan unit cost data for six of the tanning materials most commonly used for sole leather. The actual tan unit cost is obtained by adding to the initial tan unit cost the cost of the tannin lost by fermentation, and the ultimate tan unit cost by adding to the actual tan unit cost the cost of the tannin apparently lost because of low fixation values. The data are based on costs as of January, 1954, and are expressed in comparison with mangrove cutch extracts, which has the highest fixation value of all the common tanning materials.

TABLE VIII. Comparative Tan Unit Costs, in Cents, of Certain Extracts.

Extract	Price per pound	Tannin basis, %	Initial tan unit cost	Tannin loss, %	Actual tannin cost	Combined tannin	Ultimate tan unit cost
Cutch	8.50	55	15.30	0.03	15.30	69.61	15.30
Wattle	10.00	60	16.60	3.4	17.16	37.15	25.00
Chestnut	4.40	25	17.86	18.6	21.16	64.55	22.66
Quebracho	11.30	63	18.28	27.3	23.27	29.63	35.07
Hemlock	6.25	25	25.00	31.4	33.85	46.48	43.75
Oak	6.50	25	26.00	29.7	33.73	44.04	45.50

The commonly used vegetable tanning materials differ greatly in color, tanning properties, and the texture and properties of the leathers, they produce. Leather used for the soles of shoes must be thick, firm, and highly resistant to abrasive wear, and accordingly the hides must be heavily tanned, principally with those tanning materials which will produce these properties. For transmission belts, the leather must be firm, resistant to stretch, and have a high degree of tensile strength. Other leathers, such as shoe upper, upholstery, bag, and bookbinding, must also be tanned with those vegetable tanning materials that may be depended upon to give them the

right properties. Table IX shows the principal differences in the composition of normal sole, belting, and upper leathers.

TABLE IX. Analyses of Vegetable-Tanned Leather (Moisture-Free Basis).

	Sole, %	Belting, %	Upper, %
Hide substance	36.12	56.42	58.60
Water-soluble	38.73	18.82	4.90
Combined tannin	24.76	30.80	36.10
Soluble tannin	18.45	13.38	2.95
Soluble nontannin	20.28	4.98	1.95
Degree of tanning	68.60	54.60	61.40
Fixation of tannin	40.70	35.40	38.10

From the analyses of many varieties of vegetable-tanned leather, it has been estimated that the total average tannin content is about 45.0%, and the hide substance content 55.0% (moisture-free basis).

Table X gives U.S. consumption of raw tanning materials and imported and domestic extracts. Table XI shows 1952 data for the total amount of vegetable tanning material used in the U.S. together with the total amount of tannin. These data were furnished by the U.S. Department of Commerce, Leather, Shoes and Allied Products Division.

TABLE X. Consumption of Tannin from Imported and Domestic Tanning Materials (1940-1950).

Source	Total pounds	Yearly average
Raw tanning materials	382,231,361	34,748,305
Imported extracts	1,579,249,280	143,568,116
Domestic extracts	744,394,566	67,672,234
<i>Total</i>	<i>2,705,875,207</i>	<i>245,988,655</i>

TABLE XI. Consumption of Tanning Materials in the U.S. in 1952.

Material	Pounds Crude Material	Pounds Pure Tannin
Divi-divi	984,113	373,970
Hemlock	68,412	12,237
Mangrove	29,587,390	12,404,735
Chestnut	144,052,695	67,334,736
Myrobalans	15,257,850	5,430,710
Nutgalls	337,559	168,778
Quebracho	276,169,466	119,510,830
Sumac	1,366,240	371,385
Valonia	15,722,131	5,805,346
Wattle	73,385,837	59,121,456
Oak	30,000	7,500
Miscellaneous	3,490,426	2,108,967
<i>Total</i>	<i>560,452,119</i>	<i>272,650,650</i>

**Quebracho.** Although several varieties of quebracho trees are indigenous to the Argentine and Paraguay, the most valuable as the source of tannin is the heartwood of *Quebrachia lorentzii*, known as quebracho colorado. The wood contains 20-23% of easily extractable tannin of the catechol variety. Because of its high purity or low

nontannin content it produces firm leather. This is especially true of the solid extracts made in South America. However, the liquid extract made in the U.S. from imported quebracho logs, because of its higher nontannin content and lower astringency, produces a fuller and somewhat softer variety of leather than that produced from solid extract.

Quebracho extract, either in solid or liquid form, is used in some manner for the production of leather ranging from the heaviest and most solid sole leather to the very lightest sheepskin leather for shoe linings and similar purposes. It also has an important use in drilling muds.

**Chestnut Wood.** The most important domestic tanning material is chestnut wood, and especially the wood of the common chestnut oak, *Quercus prinus*, which grows profusely particularly in Virginia, North Carolina, and Tennessee. The wood contains 5–8% of tannin. Tannin solutions from chestnut oak wood give blue-black precipitates with ferric salts and respond to all reactions of pyrogallol tannin.

Chestnut extract is generally sold in the liquid form, containing 25% tannin. It is consumed mostly in the tanning of hides into sole and other heavy leathers such as belting and harness. It has a high tannin fixation value and produces a firm, thick leather. Because of its high acid content and correspondingly low pH value, chestnut wood extract is rarely used alone, but is blended with mangrove cutch, quebracho, and mangrove cutch extract.

**Divi-divi.** Divi-divi is the pod of a tree, *Caesalpinia coriaria*, that grows in northern South America and Mexico. It grows from 20 to 30 ft. in height and 21 in. in diameter. The pods are about 1 in. broad and 3 or more inches long. There is little or no tannin in the bean, but pods of good quality contain 40–50%. The tannin is of the pyrogallol variety. The principal value of divi-divi to the tanner is its ready fermentability.

**Myrobalans.** Myrobalans is the name given to the unripe fruit or nuts of various species of the tree *Terminalia chebula*, indigenous to the Malay Archipelago. The nuts contain 30–40% tannin of the pyrogallol variety. Its chief value for tanning purposes is its ready fermentability and acid-forming properties. Myrobalans are used chiefly in sole leather tanning because they produce a tanning liquor comparatively low in pH value.

**Mangrove Cutch.** Mangrove bark cutch extract is made from the bark of the genus *Rhizophora*. These trees grow in the salt marshes along the coast and mouths of the rivers of most of the islands of the Malay Archipelago. The principal sources, at the present time, are British North Borneo and the Philippine Islands.

The bark contains 35–40% of a peculiar form of catechol tannin. The tanning extract contains 55% tannin, which is free from insolubles and may be used without any chemical treatment. Because of its high lactic acid content it produces the plumpest leather and, in addition, has the highest tannin fixation value. Because of their remarkable resistance to fermentation, loss of tannin, and freedom from sludge, mangrove cutch tanning liquors are the most economical for all varieties of vegetable-tanned leather.

**Wattle Bark.** Wattle bark is obtained from certain trees of the genus *Acacia*, such as *A. longifolia*. It is one of the richest tannin-bearing barks known, containing 37–40% tannin. Most of the wattle bark, either in the form of raw bark or as solid extract, is imported into the U.S. from British East Africa and the Union of South Africa.



Wattle bark liquor is rarely used alone because it produces a soft variety of leather. However, its use is increasing steadily in sole and heavy leather tanneries, principally for reducing the astringency of quebracho. It has a tendency to raise the tannin fixation value of quebracho and certain other extracts.

**Valonia.** Valonia oak, *Quercus aegilops*, grows profusely in Albania, Greece, the Greek Archipelago, Asia Minor, and Palestine. The tannin, valonia, is found in the cups and beards of the acorn. The beards contain about 40% tannin, the cups usually rather less. Valonia yields a pyrogallol tannin and is used principally in the tanning of sole leather, in the natural state; its chief value is its acid- and bloom-forming properties.

**Gambier.** Gambier, or terra japonica, is the tannin obtained from the leaves and twigs of the Malayan shrub *Uncaria gambir*. It comes to market in cakes called "block-gambier," containing 35-40% tannin, or in cubes containing 50-65%.

**Gallnuts.** Turkish or Aleppo galls are found on the leaves and twigs of the species of oak called *Quercus infectoria*. The gallnuts contain 50-60% gallotannin. Chinese gallnuts are usually found on a species of sumac and are a valuable source for tannin.

Gallnut liquors and extracts produce light-colored leather. However, the use of gallnuts for tanning is comparatively unimportant.

**Hemlock Bark.** Hemlock bark was formerly one of the most widely used of American tanning materials. The best variety, derived from *Tsuga canadensis* or *Abies canadensis*, contains 8-12% of some form of catechol tannin. Depending on the methods used in leaching or extracting, hemlock liquors produce leather which varies in color from light tan to dark red.

The principal use for hemlock bark liquors is in the tanning of hides for upholstery, bag, case, and strap leathers. The best results are obtained from the liquors prepared from the direct leaching of hemlock bark. However, considerable quantities of 25% extract are made at the present time.

**Sumac.** The principal kind of sumac used in the tanning of leather is that obtained from the leaves and small twigs of the Sicilian shrub *Rhus coriaria*. Good sumac contains 25-27% pyrogallol tannin. It is used principally for the production of light-colored sheepskin leather. Formerly, large quantities were used for making morocco leather from kid and goat skins.

*Rhus typhina* grows in the U.S. and is called Virginia or Staghorn sumac. It contains 10-18% tannin and produces a much darker-colored leather than that obtained from Sicilian sumac.

**Oak Bark.** During the early years of the 19th century the principal tanning material used in America was oak bark. The most valuable bark is that obtained from the chestnut oak or *Quercus prinus*, which contains 10-14% of a tannin known as quercitannin. It is a mixture of 75% of a catechol tannin and 25% of a pyrogallol tannin. It gives green-black precipitates with ferric salts, and, in all its principal reactions, it behaves like a catechol tannin.

### Bibliography

- (1) Hilbert, F. L., "Vegetable Tanning Materials," *Hide and Leather*, May 18, 1938.
- (2) Hilbert, F. L., "The Tannins," *Chem. Inds.*, 375, 505, 1939.
- (3) Orthman, A. C., *Tanning Processes*, Hide and Leather Publishing Co., Chicago, 1945.
- (4) Procter, H. R., *Principles of Leather Manufacture*; also *Leather Industries Laboratory Book*, E. and F. N. Spon, 1908.

- (5) Seltzer, J. M. and Marshall, F. F. *J. Am. Leather Chemists' Assoc.*, 168, 1930.
- (6) Wilson, J. A., *Chemistry of Leather Manufacture*, Chemical Catalog Co., 1928.
- (7) Wilson, J. A., and Merrill, H. B., *Analysis of Leather and Material Used in Making It*, McGraw-Hill, N.Y., 1931.
- (8) Wilson, J. A., *Modern Practice in Leather Manufacture*, Reinhold, N.Y., 1941.

F. L. HILBERT

### VEGETABLE TANNING MATERIALS—CHEMISTRY

Since the chemistry of the vegetable tanning materials is little known and their properties depend somewhat upon the method of extraction, they will be referred to in this discussion as vegetable tanning extracts rather than as "tannins," for this word has the implied connotation of a chemical structure. All tanning extracts thus far examined contain mixtures of polyphenolic substances, and some have associated with them certain sugars (whether as an integral or necessary part of the structure is not known). They give a positive test with typical phenolic hydroxyl reagents and precipitate gelatin from water solution, but, since these tests are also positive for many materials which do not exhibit tanning properties, they cannot be used to categorize tanning materials. The only reliable method of ascertaining whether a given material is a tanning extract is to treat untanned skin with it under proper conditions and to observe whether leather results. For commercial purposes a complex chemical analytical method of determining the percentage of "tans" and "non tans" in an extract has been in international use for over 50 years; it involves the reaction of an extract with specially prepared and standardized hide powder under very precisely specified conditions (7).

Our knowledge of the structural chemistry of the constituents of vegetable tanning extracts is very limited for several important reasons:

(1) Variations in the method of extraction of the plant material produces different mixtures and may result in the polymerization, depolymerization, or other chemical changes of the materials originally present in the plant.

(2) Various chemists assumed that there was present a definite tanning molecule that was responsible for the tanning power of the extract, and postulated many structural analyses based on the C, H, O content, which of course has no validity in mixtures.

(3) All extracts contain mixtures of polyphenolic substances which because of their high polarity are not readily separable by usual organic techniques; also the phenolic hydroxyl groups mask the reactivity of possible other groups present.

(4) Changes take place upon aging, heating, or treatment of the extract with various chemicals which make separation techniques dubious.

(5) Thus far no crystalline materials have been obtained from the extracts (except degradation products with no tanning ability).

(6) All degradation products that have been obtained and identified to date are much too simple to indicate the original structure from which they came.

(7) Molecular weight determinations based on colligative properties (freezing point, etc.) of substances capable of strong association (hydrogen bonding) in polar solvents have no validity.

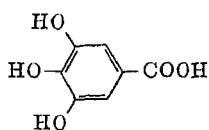
(8) The extracts may contain mixtures of substances which in a purified form are water-insoluble but which are mutually soluble in the tanning extract, and these mixed materials may be important in the tanning properties of the extract.

(9) No materials have been synthesized which have been shown to be identical with substances in the tanning extracts.

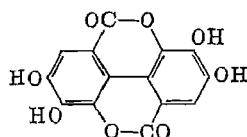
Before about 1945, our knowledge of the chemistry of tanning extracts was due primarily to the investigations of Fisher (2), Freudenberg (4), Nierenstein (9), and Russell (12). As a result of this work the natural tanning extracts were classified into two main groups: the hydrolyzable tannins and condensed tannins. The *hydrolyzable tanning extracts* yield water-soluble products upon hydrolysis with boiling dilute mineral acid, whereas the *condensed tanning extracts* form precipitates known as "tanners red" or *phlobaphene* under these conditions. This classification corresponds fairly closely to the classification into pyrogallol and catechol tannins, in the earlier literature. Most tanning extracts fall into the condensed or phlobaphene category, but even these extracts may contain various amounts of the hydrolyzable tanning group.

### Hydrolyzable Tanning Extracts

The hydrolyzable tanning extracts have been further subdivided into two groups: one yielding gallic acid (*q.v.*), 3,4,5-hydroxybenzoic acid (I) and glucose upon hydrolysis, and the other giving ellagic acid (II) and glucose. The first group are known as gallotannins, and the second as ellagitannins.



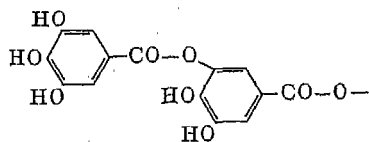
(I) Gallic acid



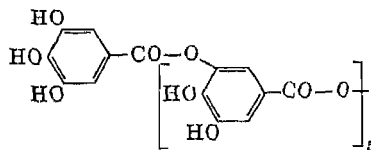
(II) Ellagic acid

**Gallotannin Extract (Gallotannic Acid; Tannic Acid).** Gallotannin extract comes chiefly from pathological growths, called galls, present on the leaves and buds of certain species of oak and sumac. The chief commercial sources are Chinese and Aleppo galls. Various amounts of this material may also be present in other hydrolyzable and condensed tanning extracts. See also *Astringents*.

After many years of work on this material Fisher and Freudenberg (3) suggested two possible structural formulas for gallotannic acid based on a material which they considered to be "purified" tannin from the original extract. In one of them, the five hydroxy groups in  $\alpha$ - or  $\beta$ -D-glucose (see Vol. 2, p. 874) are replaced by the radical "*m*-digalloyl" (III). In the other, four hydroxyl groups are replaced by galloyl,  $C_6H_2(OH)_3COO-$ , and the hydroxyl group at position 6 by a hexagalloyl radical (IV).



(III)



(IV)

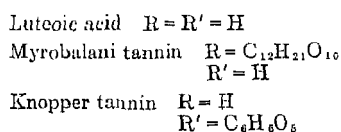
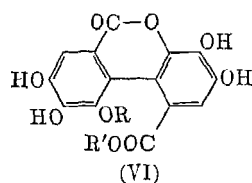
These workers synthesized penta-*m*-digalloyl- $\alpha$ - and - $\beta$ -glucose but were unable to show that either of these products was identical with the "purified" gallotannin. A further discrepancy of these formulas with experiment appears in the glucose content.



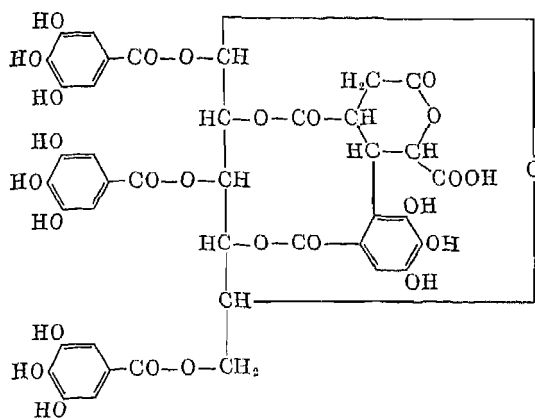
terial by a known route and prove the identity of the synthetic with the naturally occurring material.

**Ellagitannin Extracts.** The class of hydrolyzable tanning extracts which yield ellagic acid (II) upon hydrolysis is represented by myrobalans, divi-divi, algarrobbilla, and valonia.

*Myrobalans Extract.* Nierenstein (8) obtained from myrobalans extract a crystalline substance, which he called myrobalani-tannin, and which upon enzyme hydrolysis yielded luteoic acid (from which ellagic acid could be derived by lactone formation) and two moles of glucose. This crystalline material gave a positive test for tanning action and analyzed by the commercial method as 98–99% tannin. Nierenstein assigned to it the formula for luteoic acid with a diglucoside radical,  $C_{12}H_{21}O_{10}$ , attached as shown in (VI). Another substance in myrobalans extract was isolated in a crystal-



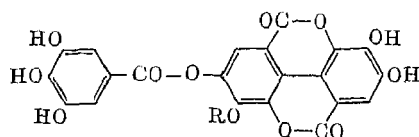
line form and has been called chebulinic acid; it yielded on hydrolysis gallic acid, glucose, and an unknown oxygen-rich component. Schmidt (15) has modified the conclusions from the earlier studies of chebulinic acid and proposed the structure (VII).



(VII) Chebulinic acid (Schmidt)

Recent work by White (17) using two-dimensional paper chromatography has shown at least ten major constituents present in myrobalans extract, whereas only four (gallic acid, ellagic acid, myrobalani-tannin, and chebulinic acid) have been isolated and identified in work thus far. Asquith (1), using solvent fractionation followed by paper chromatography, has found digalloylglucose, gallic acid, chebulinic acid, pyrogallol, ellagic acid, and five unidentified compounds, thus confirming the great complexity of myrobalans extract.

*Other Ellagitannin Extracts.* Hydrolyzable ellagitannin extracts other than myrobalans have not been thoroughly studied, but several structural formulas have been suggested based on hydrolysis products and reactivity. Freudenberg and co-



(VIII)

Divi-divi tannin  $R = C_{14}H_{11}O_{11}$

Chestnut-wood tannin  $R = C_{10}H_6O_6$

workers (5) suggested the structures in (VIII) for divi-divi tannin and chestnut wood tannin. Nierenstein (9) attempted to prepare the dimethylated derivative of ellagic acid by methylation of divi-divi and subsequent hydrolysis, but was unsuccessful, thus casting some doubt on the formula proposed above.

Nierenstein suggested that Knopper tanning extract (from galls on aconus) is a glucoside of luteoic acid (V) with about four luteoic acid residues per glucose unit.

Chromatographic work by White (17) on various ellagitannin extracts has shown them to be much more complex mixtures than indicated by the structural formulas shown here. Chestnut and valonia exhibit somewhat similar patterns, but both show at least twelve different substances present. All the hydrolyzable tannins examined by paper chromatography show the presence of gallic and ellagic acids in addition to many unidentified substances.

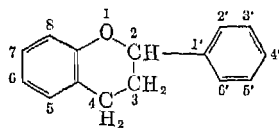
### Condensed Tanning Extracts

Most commercially important tanning extracts fall in the category of condensed or phlobaphene tannins, and these occur generally in the wood, bark, and roots of plants. Among these extracts may be listed: cutch, gambier, quebracho, wattle (mimosa), canaigre, eucalyptus, hemlock, spruce, beech, and mangrove.

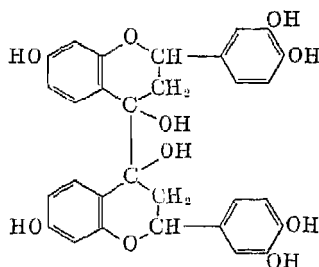
These tanning extracts all form an insoluble phlobaphene upon heating with dilute mineral acid, in contrast to the hydrolyzable tanning extracts, and they all give positive tests for phenolic hydroxyl groups. Our knowledge of the structural chemistry of the tanning materials present in these extracts has come more from inference than from experimental proof, and recent investigations which have shown the great complexity and extreme heterogeneity of the extracts casts considerable doubt on the validity of any structural formulas so far suggested.

The breakdown products obtained from condensed tanning extracts degradation have been the basis for most structural hypotheses. The products obtained always consist of a polyhydroxy phenol (phloroglucinol, resorcinol, or pyrogallol) and a phenolic acid (protocatechuic or gallic acid). Roux (13) and Putnam (10) have recently reviewed the identified degradation products obtained from wattle extract and quebracho extract respectively. Most workers have assumed that the flavan structure (IX) best represents the structural skeleton of the tanning molecule, mainly because one naturally occurring flavan (catechin) has been found in both gambier and cutch extracts. It should be noted, however, that catechin is not a tanning agent, nor are other synthetically prepared flavans; that catechin has not been converted into a tanning agent as yet; that no flavan has been isolated from any of the many other condensed tanning extracts except cutch and gambier; that no other proof of the flavan structure has so far been found.

Many unproved structures for condensed tannins have been offered by various investigators. The work of Russell (12) should be treated more closely because he was able to synthesize substances which had properties qualitatively identical with



(IX) Flavan

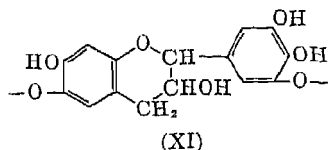


(X)

those of natural tanning extracts. These were, unfortunately, amorphous materials, but they were prepared by a fairly straightforward route and it is possible that they represent the types of compounds present in natural tanning extracts. He prepared and identified 2',3,4,4'-tetrahydroxychalcone (butein), which yielded an amorphous tanning material on reduction with zinc dust in alcoholic acid. Russell considered this material to have the structure of a bis-flavpinacol (X). He subsequently synthesized some ten bis-flavpinacols with various substituents on various positions of the benzene rings and concluded that any bis-flavpinacol with 3',4'-hydroxyl groups is tanning agent. This work, however, offers no proof that the natural tanning extracts contain substances of this bis-flavpinacol structure.

Putnam (11) was able to obtain two degradation products from quebracho extract which were of larger molecular size than those previously reported for condensed tannins. He has reported their basic empirical formulas to be  $C_{22}H_{20}O_9$  and  $C_{23}H_{20}O_8$  but as yet has not been able to identify these materials structurally.

Roux (13,14) has postulated a condensation product involving ether linkages between flavan units (XI) giving rise to a linear polymer of five or six flavan units (with hydrogen atoms as the end groups).



(XI)

The work of White and co-workers (17), Asquith (1), and Roux (14) on the fractionation of the condensed tanning extracts by various techniques indicates quite clearly that the problems of the structural chemistry of vegetable tanning extracts are far from solved. White has shown by two-dimensional chromatography that cutch, gambier, quebracho, wattle (mimosa), canaigre, and eucalyptus tanning extracts contain mixtures of many polyphenolic substances. He was able, by counter-current fraction using immiscible solvents followed by two-dimensional chromatography, to show the presence of some twenty-seven different polyphenolic materials in wattle extract. When separation techniques have been developed and employed to obtain sufficient quantities of single substances for adequate structural analysis, then perhaps we shall be in a better position to understand the structural chemistry of the condensed tanning extracts. It seems certain that no single structure can explain all the substances so far isolated in these extracts.

## Bibliography

- (1) Asquith, R. S., *J. Soc. Leather Trades' Chemists*, **36**, 316 (1952).
- (2) Fisher, E., *Untersuchungen über Depside und Gerbstoffe, 1908-1919*, Springer, Berlin, 1919.
- (3) Fisher, E., and Freudenberg, K., *Ber.*, **45**, 915 (1912); Freudenberg, K., *Die Chemie der natürlichen Gerbstoffe*, Julius Springer, Berlin, 1920.
- (4) Freudenberg, K., *Tannin, Cellulose, Lignin*, Springer, Berlin, 1933.
- (5) Freudenberg, K., and Walpolski, H., *Ber.*, **54**, 1695 (1921); Freudenberg, K., and Fick, B., *Ber.*, **53**, 1728 (1920).
- (6) Hillis, W. E., *J. Soc. Leather Trades' Chemists*, **37**, 390 (1953).
- (7) *J. Am. Leather Chemists' Assoc.*, **49**, 174 (1954).
- (8) Nierenstein, M., *Ber.*, **43**, 1267 (1910).
- (9) Nierenstein, M., *The Natural Organic Tannins*, Sherwood Press, Cleveland, Ohio, 1935.
- (10) Putnam, R. C., and Gensler, W. J., *J. Am. Leather Chemists' Assoc.*, **46**, 613 (1951).
- (11) Putnam, R. C., *J. Am. Leather Chemists' Assoc.*, **48**, 368 (1953).
- (12) Russell, A., *Chem. Revs.*, **17**, 155 (1935).
- (13) Roux, D. G., *J. Soc. Leather Trades' Chemists*, **36**, 393 (1952).
- (14) Roux, D. G., *J. Soc. Leather Trades' Chemists*, **37**, 229 (1953).
- (15) Schmidt, O. T., *Das Leder*, **6**, 127 (1954).
- (16) Sunthakar, S. R., and Jatkar, S. K. R., *J. Indian Inst. Sci.*, **21A**, 209 (1938).
- (17) White, T., Kirby, K. S., and Knowles, E., *J. Soc. Leather Trades' Chemists*, **36**, 148 (1952).
- (18) White, T., *J. Soc. Leather Trades' Chemists*, **33**, 39 (1949).

R. L. STUBBINGS

## SYNTHETIC TANNING MATERIALS

The term syntan as used commercially refers to a broad group of manufactured materials that may be used as adjuncts to or as partial or complete replacements for natural vegetable tanning extracts. In general they are amorphous, water-soluble materials that may be obtained either in concentrated water solution or in powder form, and they range from colorless to dark brown. Most commercially important syntans are condensation products of formaldehyde and one of the following classes of materials (water solubility may either be inherent in the condensed product or may be produced by addition of certain groups to the condensed product): naphthalene-sulfonic acids, various phenols and sulfonated phenols, diaryl sulfones, urea, melamine, and dicyandiamide. Some syntans are produced without formaldehyde condensation from materials such as: styrene-maleic anhydride, aryl diisocyanates, and lignin sulfonates. In addition to the above-mentioned materials, methods of tanning have been developed in which materials similar to syntans are formed in the skin during the leather-making process.

M. Nierenstein, during his studies on the condensation reactions between formaldehyde and phenols, found in 1905 that in many cases the derivatives gave precipitates with gelatin and otherwise acted like tannin. Stiasny confirmed Nierenstein's findings and suggested the possibility of preparing artificial tanning materials. Stiasny obtained German Patent 262,558 (1913) and U.S. Patent 1,337,405 (1917) for materials that he called syntans, a contraction of *synthetic tannins*. They were introduced into the U.S. by the Badische Anilin und Soda Fabrik under the trade names Neradol D and Neradol N. The former was produced from crude cresols, and the latter from naphthalene. At first the syntans were looked upon with much disfavor in the U.S., but about 1921 Rohm & Haas began to manufacture Leukanol along the lines of Stiasny's patents.

Table I gives U.S. production and sales of synthetic tanning agents for 1953 (U.S. Tariff Commission).



TABLE I. U.S. Production and Sales of Synthetic Tanning Agents, 1953.

	Production, thousand pounds	Sales		
		Thousand pounds	Thousand dollars	Value per lb.
2-Naphthalenesulfonic acid-formaldehyde condensate and salts	22,187	20,626	3,342	0.16
Other naphthalenics	2,597	2,385	351	0.15
Other synthetic tanning materials <sup>a</sup>	11,009	10,799	2,969	0.27
<i>Totals</i>	<i>35,793</i>	<i>33,810</i>	<i>6,622</i>	<i>0.20</i>

<sup>a</sup> Including lignin sulfonic acid salts, styrene-maleic anhydride copolymer, bis-phenol-formaldehyde-bisulfite condensate, phenol-formaldehyde condensate sulfonated, diphenyl sulfone disulfonic acid-formaldehyde condensate, and others.

In a comparison of the syntans and the natural vegetable tanning extracts, the most striking feature is their complete lack of similarity in chemical nature. The reason for this is economic because to be competitive, any syntan must be relatively inexpensive and synthetic products corresponding chemically with the natural tannins would be very costly.

Historically the development of syntans has been closely connected with national security, because most nations which consume large quantities of tanning agents must import a large proportion of these materials, and therefore during restricted trade periods (World Wars I and II) interest in the synthetic products increased. As a result of wartime developments some of the products attained a permanent place in the tanning industry even after free trade was resumed.

Most of the research work in syntan chemistry has been directed along the lines of product development and use. A large proportion of this work has been conducted by the manufacturing companies and has been released only in the form of patent disclosures. However, detailed information about the manufacture of syntans in Germany has been collected by Allied investigation teams and released in government reports (8). Several independent investigations on materials and methods of production of syntans have appeared (2,7,15,18). Reviews of historical and industrial data on syntans (3) and of their general chemistry (13) have appeared, and a book on the subject (4) has been published.

Information on the chemical constitution of the commercial syntans is woefully lacking. It is thought that they consist of mixtures of various molecular weights and molecular structures but few attempts to separate and identify pure materials have been reported. As a further complication, the commercial products may be mixtures of various basic syntan materials whose composition is not released by the manufacturer. The most common admixtures of this type are probably various lignin sulfonates with condensed phenolic sulfonates.

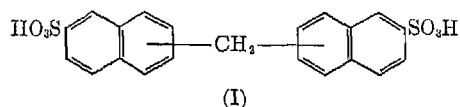
Table II lists synthetic tanning materials commercially available in the U.S. in 1954.

**Naphthalenic Syntans.** This type of syntan is by far the most important commercially used in the United States and is manufactured by condensing naphthalene-1- or -2-sulfonic acid with formaldehyde. The actual structure has not been determined, indeed the product is probably a mixture, but the product (from the naphthalene-2-sulfonic acid) may be represented by (I). This material, in contrast to all the natural tannins, has no hydroxyl groups and therefore must react as a tanning agent entirely differently from the natural products. It has been suggested that this material reacts

TABLE II. Commercially Available Syntan Products.

Company	Trade names	Remarks
<i>Naphthalenic Syntans (adjuncts to vegetable tans, retannage of chrome leather, mordant for dyeing)</i>		
American Cyanamid Co.	Tanak A, L, DN, CNS	neutral salt form
	Tanak AA, SC, BB, DCX	acid form
American Dyewood Co.	Adeotan NNC	neutral salt form
	Adeosyntan NNC	acid form
Chemtan Co.	Chemtan C	strong acid form
Monsanto Chemical Co.	Mertanol	
National Aniline Division, Allied Chemical and Dye Corp.	Naccotan A	
Nopeo Chemical Co.	Nopeo 1187 X	neutral salt form
A. J. & J. O. Pilar Co.	Trutan OA	acid form
Rohm & Haas Co.	Leukanol, ND, HPS, PC	acid form
	Tamol N, L	neutral salt form
Jacques Wolf & Co.	Tanasol	
<i>Aromatic Hydroxy Syntans (used as partial or complete replacements for vegetable tans; may be mixtures)</i>		
American Cyanamid Co.	Suprak 57	bis-phenol-formaldehyde-bisulfite condensate
	Suprak 58	phenolic replacement
	Suprak 59	phenol-formaldehyde-bisulfite condensate
Chemtan Co.	Chemtan Y-1, Y-2, Y-3, Y-4	phenolic replacement
A. J. & J. O. Pilar Co.	Trutan T, PA, S55, R108	phenolic replacement
Reilly-Whiteman-Walton Co.	Microtan 80, 150	phenolic replacement
Rohm & Haas Co.	Leukanol R	phenolic
	Orotan TV	phenolic replacement
Jacques Wolf & Co.	Synektan	phenolic
<i>Nitrogen Resin Syntans (primarily for retannage of chrome-tanned leather, white and pastel shades)</i>		
American Cyanamid Co.	Tanak MRX	trimethylolmelamine
Chemtan Co.	Chemtan R-6, R-12, R-41	diacyandiamide-formaldehyde partial polymer
<i>Lignin Sulfonates (similar in use to naphthalenic syntans, as additives and pretannages with vegetable tans)</i>		
Robeson	Liquid spruce	
International Paper Co.	Bindarene Flour	
Mead Corp.	Meadol	
Marathon Corp.	Marathon Tan A	
West Virginia Pulp and Paper Co.	Indulin	
<i>Miscellaneous Syntans</i>		
Du Pont Co.	Cl-942	styrene-maleic anhydride copolymer, for added fullness in retannage of chrome leather
General Dyestuff Corp.	Leotan A	methyl vinyl ether-maleic anhydride copolymer

entirely ionically through the anionic sulfo groups with the charged basic groups of the protein, whereas vegetable tannins react primarily through their phenolic hydroxyl groups (14). Therefore naphthalenic syntans only react as tanning agents at low pH



levels (below pH 3) and cannot be used in the same manner as, or as complete replacement for, vegetable tanning extracts.

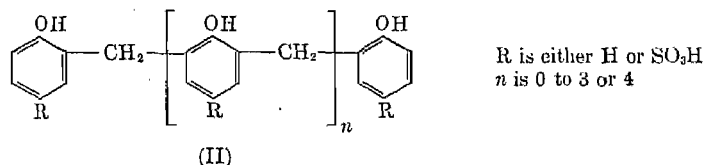
Various manufacturers produce naphthalenic syntans and usually in either an acid form or a salt form (Table II). The producers have recommended them for the following uses in leather production: (1) for chrome-tanned leather: as a pretannage, neutralizing agent, bleach for white leather, dispersing agent for resin retannage, leveling agent for acid and direct dyes, and as a mordant for basic dyes; (2) for vegetable-tanned leather: as a pretannage, as an additive to the vegetable tanning extracts to prevent sludge formation, and to increase the penetration of the vegetable tannins, as a bleach to clear the grain.

In addition to their uses in the leather industry, naphthalenic syntans have been recommended: (1) as pigment dispersants in the manufacture of paper and printing ink; (2) for ceramic molding; (3) as carbon black dispersant in the rubber industry; (4) as an additive to portland cement for increasing durability and waterproofness; (5) for the manufacture of sutures; (6) as bleaching agents for paper pulp.

**Aromatic Hydroxy Syntans.** This class of syntans generally have greater tanning power than the naphthalenic types, and some products in this category may be used as complete replacements for natural vegetable tannins in heavy leather manufacture. Several basic materials of this class are produced commercially which differ in starting materials and methods of condensation and solubilization. The names of the specific materials used for these products and information about whether they are mixtures or single syntans have not been released by the manufacturers, nor have they been reported on independently, so they can only be reported as belonging in general to the class of aromatic hydroxy syntans (see Table II).

From independent investigations and various patent disclosures, however, some general information about the chemical raw materials and methods of condensation can be tabulated.

There are two general methods of production of these syntans; (1) the sulfonation of an aromatic hydroxy compound followed by condensation with formaldehyde, and (2) the condensation of an aromatic hydroxy compound with formaldehyde followed by sulfonation to make the product water-soluble. An illustration of the general type of compound formed is shown for phenol in (II), although again probably a mixture of products is formed with various molecular weights, and with various ratios of sulfonic acid groups to phenolic hydroxyl groups.



For commercial syntans the starting materials may be phenols (usually phenol or cresol), naphthols, bis-phenols, hydroxydiphenyl sulfones, etc., and of course the mixture of products obtained depends upon the conditions of the condensation and sulfonation. As in the case of the naphthalenic syntans, no information has been published concerning the chemical species and the ratios present in the commercial syntan products. However, considerable work (2,15,18) has been done relating the methods of sulfonation and condensation to the value of the mixed products as tanning agents.

The general conclusions from these investigations are:

(1) Formaldehyde condensation products of aromatic hydroxy sulfonic acids have good tanning power but lack filling properties, so they are generally not suitable as complete replacements for vegetable tanning extracts in heavy leather manufacture.

(2) Products formed by partially sulfonating the formaldehyde condensation product of a hydroxy aromatic compound have better tanning power and greater filling action than the products mentioned in (1).

(3) Formaldehyde condensation products of polyphenols (which are water-soluble without sulfonation) have excellent tanning and filling properties.

(4) Increasing the degree of condensation with formaldehyde first increases the tanning power and then decreases it.

(5) Increasing the degree of sulfonation decreases the tanning ability (only enough sulfonation should be effected to make the product water-soluble).

(6) The presence of the hydroxyl group in syntans formed by method (1) above has little effect on the tanning power, since methylated materials were found to be almost as good as their free hydroxyl counterparts. However, the hydroxyl group is very important in syntans prepared by method (2) since the methylated products had very little tanning action.

(7) Increasing the acidity of the phenolic hydroxyl increases the tanning power; for example, this may be done by introducing a sulfone group (as *p-p'*-dihydroxydiphenyl sulfone) and then condensing with formaldehyde.

(8) Better materials are produced by condensing mixtures of sulfonated and unsulfonated compounds than by condensing either fully sulfonated or partially sulfonated materials with themselves. The tanning power is dependent on both the number and the position of the phenolic hydroxyl groups and is better if the product contains one or more unsulfonated phenolic rings per molecule.

(9) Lignin sulfonates may be combined with aromatic hydroxy syntans to produce cheaper materials that are still adequate as complete replacements for vegetable tanning extracts. The best of these materials employs a furfural condensation product of resorcinol as the phenolic sytan.

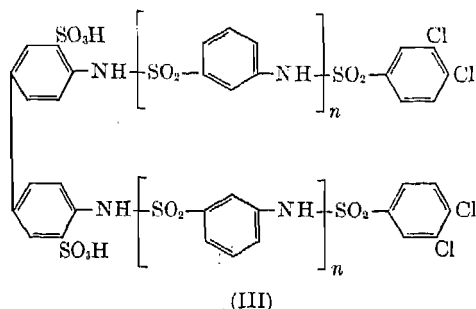
(10) Products made according to the procedures outlined in sytan patent disclosures are generally unsatisfactory as tanning agents. (Some 200 materials made based on 40 patents showed only 5 that had good tanning properties.)

The diphenyl sulfone type of syntans are reported to be more resistant to yellowing than the corresponding phenol-formaldehyde types and are recommended therefore for white and pastel-colored leathers.

Some additional chemical types of aromatic hydroxy syntans have been mentioned, but it is not known whether any of these materials are now being produced commercially. The use of urea along with formaldehyde as a condensing agent for a sulfonated phenolic material produces a sytan whose basic structure as suggested by Short (13) may consist of benzene nuclei, each with a hydroxyl group, connected together in a chain of indefinite length by  $-\text{CH}_2\text{NHCONHCH}_2-$  linkages, and with a variable number of  $\text{SO}_3\text{H}$  groups. This type of material is said to have slightly better tanning power than its simple formaldehyde counterpart, and to have very good resistance to light.

Sulfonamide-type syntans have also been prepared in which the exact chemical structure is known because the molecule is built up by unambiguous stages. A structure of this type is shown in (III), and the material is reported to have excellent tan-

ning properties especially if built up to a molecular weight corresponding to the natural tannins (about 1,500-2,500).



**Lignin Sulfonate Syntans (Spruce Extract, Sulfite Cellulose).** Because the waste liquor from the sulfite treatment of wood pulp has been known to react with skin fiber, and because of its extremely low cost, much interest has centered on the possibility of utilizing this material either directly in tanning extracts, or by producing suitable tanning materials by chemical modification of the material, or in mixture with other types of syntans to reduce the cost. The lignin sulfonate material is often referred to commercially as "spruce extract" and also as "sulfite cellulose," incorrectly, since the cellulosic components of the wood are not present in the waste liquor.

Investigations by Baum and co-workers (1) and by Kremen (9) and Lollar (10) indicate that lignin sulfonates used alone are very poor tanning agents although they are taken up by the skin fiber. The reaction seems to be primarily an ionic one between the sulfonic acid groups of the lignin and the basic groups of the skin fiber, similar to that of naphthalenic syntans. The sulfite waste liquor contains a mixture of lignin sulfonates and carbohydrates, and various methods have been recommended for isolating the higher-molecular-weight lignin sulfonates, which appear to be more valuable as tanning agents. The lignin sulfonate molecules probably consist of polymers of propyl-guaiacyl units of various molecular weights. Used alone, the lignin sulfonates have been recommended for much the same purposes as the naphthalenic syntans (see above).

Many different chemical treatments have been suggested to convert lignin sulfonates into better tanning materials. Among these the most successful have been combinations or condensations with phenolic syntans (see "Aromatic hydroxy syntans" above).

**Nitrogen Resin Syntans.** The nitrogen resin syntans based on urea, melamine, or dicyandiamide are distinctly different in their use and application from the naphthalenic and phenolic syntans previously discussed. The commercial product usually consists of the monomer or partial polymer unit of the resin, which is then introduced into the skin fibers and polymerized in place by acid catalysis. For example, trimethylolmelamine (the condensation product of formaldehyde and melamine) is the monomer unit for one type of commercial material, and it has been shown that this molecule condenses with acid to form linear polymers (still water-soluble) of 10-20 monomer units (5). See *Amino resins and plastics*. The polymer unit probably reacts with the skin fiber through its methylol groups and various basic groups on the fiber.

These materials have been recommended mainly as a retannage for chrome-tanned leather and are said by the manufacturers to improve the fullness of the leather

and to improve the normally loose areas of the skin. They are particularly recommended for retannage of chrome leather to be made in white and light shades.

**Other Resin Syntans.** A high-molecular-weight polymer based on styrene-maleic anhydride which has carboxylic groups has been recommended for tannage of lightweight skins, especially for light colors. No reports are available concerning either the chemistry of the resin itself or its reaction with the animal skin fibers, but the recommended processes for using the resin indicate that it is not a tanning agent by itself but that it can be fixed in the skin by a metallic tanning salt, thus contributing toward filling up the leather (6).

A dialdehyde-resin tannage (17) has been developed in which a dialdehyde is first reacted with the skin fiber, and there is then introduced a resin former, in either monomeric or partially polymerized form, which further reacts in the skin to form a higher polymer. Urea and formaldehyde mixtures have been used as the resin former.

Another type of resin tannage using formaldehyde and resorcinol (16) and forming a syntan in the skin has been developed. In this method both reagents are applied at the same time to the skin fiber, and the condensation conditions are controlled by time and pH. The reaction that takes place is probably similar to the condensations discussed for the preparation of aromatic hydroxy syntans, with the further possibility of the excess formaldehyde linking the phenolic polymer to the skin fiber through methylene bridges.

**Water-Insoluble Syntans.** In the normal connotation a syntan is thought of as a water-soluble material, and yet there are many materials which have tanning properties and are water-insoluble. There are two general methods of effecting tannage with these materials: (1) emulsification of the tanning agent with subsequent application to the skin (same type of treatment as introducing fat or oil into leather); (2) use of an organic solvent tannage instead of a water tannage. Among the materials suggested as tanning agents in this group are the aliphatic isocyanates (see Vol. 10, p. 398). The chemical reaction that takes place when the isocyanate reacts with the skin is not well understood, but it has been suggested (11) that a polymerization of the isocyanate by reaction with water and release of carbon dioxide is involved. Also a reaction of the polymer probably takes place with the basic groups of the fiber.



Various phenolic resins, similar to the aromatic hydroxy syntans described above but of a water-insoluble type, have been found to cause a tannage when applied in an organic solvent to dehydrated animal skin.

Long-chain aliphatic sulfonyl chlorides,  $\text{RSO}_2\text{Cl}$ , have also been demonstrated to cause a tannage when applied to animal skin along with an emulsifying agent (12). It is thought that the sulfonyl chloride groups reacts with basic groups on the fiber to form sulfonamide links. These materials are prepared by treatment of hydrocarbons with sulfur dioxide and chlorine in the presence of actinic light and usually are a mixture of products.

**Resins Used as Filling Agents.** In addition to the syntan materials discussed above, which effect an actual tannage of the animal skin, resins of various types may be used to change the properties of leather without being able to cause any tannage themselves. These will be only briefly discussed here because they do not properly

belong in the category of syntans. However, their application and effects (except for the tannage) are in many cases very similar to the syntans.

Many types of resinous materials may be incorporated into leather in such a manner that they cannot be readily removed, and various materials have been recommended to increase the wear resistance, as filling agents to increase the plumpness, as waterproofing materials and so on. These resins may be applied as resin emulsions or latexes (prepared by emulsion polymerization of the monomer), as monomers or partial polymers polymerized further in the skin, as solutions of polymers in organic solvents, and so on. Among the materials which have been reported to have been applied to leather are included: natural rubber, synthetic rubbers, polysulfide liquid polymers, all types of emulsion polymers such as polystyrenes, acrylonitriles, acrylates and methacrylates, polyvinyls, and silicones.

### Bibliography

- (1) Baum, M., Lovin, R., and Salversen, J. R., *J. Am. Leather Chemists' Assoc.*, **47**, 269 (1952).
- (2) Biedermann, R., *Colloquiumsber. Insts. Gerbereichemie tech. Hochschule Darmstadt*, **5**, 25 (1949).
- (3) Blackadder, T., and Somerville, L., *J. Am. Leather Chemists' Assoc.*, **48**, 673 (1953).
- (4) Chen, P. S., *Syntans and Newer Methods of Tanning*, The Chemical Elements Publishers, South Lancaster, Mass., 1950.
- (5) Dixon, J. K., Christopher, G. L. M., and Salley, D. J., *Paper Trade J.* (Nov. 1948).
- (6) Du Pont, E. I., de Nemours, Grasselli Chem. Dept., Tech. Bull., "G-942 Tanning Agent," 1954.
- (7) Highberger, J. H., Bump, A. H., and O'Flaherty, F., *J. Am. Leather Chemists' Assoc.*, **43**, 307 (1948).
- (8) Johnson, K., Office of Quartermaster General, Military Planning Division, Research and Development Branch, Leather Series—Report Nos. 2 and 4 (released by Office of Technical Services, U.S. Dept. of Commerce, 1948).
- (9) Kremen, S. S., and Lollar, R. M., *J. Am. Leather Chemists' Assoc.*, **43**, 542 (1948).
- (10) Lollar, R. M., Buchanan, M. A., and Nicmeyer, D. D., *J. Am. Leather Chemists' Assoc.*, **42**, 232 (1947).
- (11) Noerr, H., and Hees, W., *Colloquiumsber. Insts. Gerbereichemie tech. Hochschule Darmstadt*, **2**, 3 (1948).
- (12) Patterson, G. H., *J. Am. Leather Chemists' Assoc.*, **44**, 2 (1949).
- (13) Short, W. S., *J. Soc. Leather Trades' Chemists*, **38**, 148 (1954).
- (14) Shuttleworth, S. G., *J. Am. Leather Chemists' Assoc.*, **47**, 603 (1952).
- (15) Stather, F., Schubert, R., and Bellman, R., *Ges. Abhandl. deut. Lederinsts. Freiberg/Sa.*, No. 5, 3 (1950); Stather, F., and Nebe, H., No. 7, 34 (1951).
- (16) Windus, W., *J. Am. Leather Chemists' Assoc.*, **47**, 87 (1952).
- (17) Winheim, A. H., and Doherty, E. E., *J. Am. Leather Chemists' Assoc.*, **45**, 122 (1950).
- (18) Wolesensky, E., *Natl. Bur. Standards (U.S.) Tech. Paper* 302 (1925).

R. L. STUBBINGS

**TANNINS.** See *Astringents*, Vol. 2, p. 205; *Tanning materials*.

**TANTALITE**,  $\text{FeTa}_2\text{O}_6$ . See *Tantalum*.

## TANTALUM AND TANTALUM COMPOUNDS

Tantalum, Ta, atomic number 73, atomic weight 180.95, falls in the fifth group of the periodic table directly below niobium (see *Columbium*), with which it is closely associated in nature and to which it is very similar in its properties. Tantalum has only one natural isotope,  $\text{Ta}^{181}$ , but several artificial radioactive isotopes have been prepared. The most common valence of the element is +5.

An announcement by Ekeberg in 1802 marks the beginning of the history of tantalum. Ekeberg's difficulty in finding a solvent for the oxide prompted him to name his new element tantalum in honor of Tantalus of Greek mythology. Since the works of Ekeberg and Hatchett (who reported the discovery of columbium) do not mention the presence of two elements (Ta and Nb) in their earth oxides, it can be assumed that they were both working with mixtures of the two elements. In 1844, H. Rose decided that there were two elements in the oxides and referred to one as tantalum and the other as niobium (for Niobe, daughter of Tantalus). The confusion was finally cleared in 1866 when Marignac made his classical contribution to the chemistry of tantalum, the separation of tantalum and niobium by means of the difference in the solubilities of their complex fluorides with potassium.

The first ductile tantalum was made by W. von Bolton in Germany in 1903, and tantalum found its first industrial use as a filament in early electric lamps. Approximately 11 million tantalum lamps were made before tungsten replaced tantalum for this purpose in 1909. From then until 1922, the uses of tantalum were confined to certain dental and surgical instruments. Tantalum was first produced in the U.S. in the laboratory of Fansteel Metallurgical Corporation, North Chicago, Ill., by C. W. Balke in 1922 and has been in continuous commercial production since that time.

## OCCURRENCE

Tantalum does not occur in nature in the free state (11). It is found in a number of minerals (see Table I) and is usually associated with niobium. The only commercially important minerals of tantalum are tantalite and columbite, which are variations of the same mineral,  $(\text{Fe}, \text{Mn})(\text{Ta}, \text{Nb})_2\text{O}_6$ . The mineral is called tantalite when its  $\text{Ta}_2\text{O}_5$  content exceeds its  $\text{Nb}_2\text{O}_5$  content. However, a columbite may be considered an ore of tantalum when the  $\text{Ta}_2\text{O}_5$  content exceeds 20%. Economic considerations determine this minimum value.

Tantalite and columbite occur in some pegmatite dikes in quantities which seldom exceed a few pounds per ton. This makes the mining of such deposits uneconomical unless other values are found in commercial quantities in the same ore. Much of the early tantalum ore was imported into the U.S. from Australia. It was mined from alluvial deposits located in the Pilbarra District in the northwestern part of the continent, and it assayed about 60%  $\text{Ta}_2\text{O}_5$ . More recently, substantial quantities of tantalum-bearing concentrates have been produced as a by-product of the tin-mining operation in the Belgian Congo. The tantalite-columbite concentrate is a product of magnetic separation and assays about 30%  $\text{Ta}_2\text{O}_5$  and an equal amount of  $\text{Nb}_2\text{O}_5$ . Slags from tin-smelting operations often contain from 4 to 12%  $\text{Ta}_2\text{O}_5$ .

Although it has been estimated that the earth's crust contains 0.003% of combined tantalum and niobium (12), which indicates that they are more plentiful than lead, cobalt, molybdenum, and tin, minerals suitable as ores of these elements are relatively scarce. In 1952, the Defense Materials Procurement Agency established a



purchase program to encourage the production of tantalite-columbite ores in which the agency agreed to purchase 15 million pounds of contained  $(\text{Ta}, \text{Nb})_2\text{O}_5$  at a fixed price schedule plus a 100% bonus to producers (4).

The Bureau of Mines *Minerals Yearbook* shows the estimated world production of columbite and tantalite during 1952 to be: columbite, 3,400,000 lb. containing 340,000 lb.  $\text{Ta}_2\text{O}_5$ ; tantalite, 95,000 lb. containing 50,000 lb.  $\text{Ta}_2\text{O}_5$ . The principal producing countries and their outputs, in pounds, are shown below:

	Australia	Belgian Congo	Brazil	Nigeria	Malaya	Southern Rhodesia	United States
Tantalite	15,720	—	49,813	—	—	10,360	—
Columbite	—	231,042	5,017	2,896,320	105,280	—	5,385

It can be seen that the number of pounds of  $\text{Ta}_2\text{O}_5$  contained in the columbite far exceeds that contained in the tantalite even though the average  $\text{Ta}_2\text{O}_5:\text{Nb}_2\text{O}_5$  ratio of the columbite was quite low. However, most of the tantalum contained in columbite appears in the ferroniobium which is made from it by direct reduction of the ore and is thereby lost as a source of pure tantalum. If a greatly improved method for the extraction and separation of niobium and tantalum from low tantalum ores and slags were developed, the tantalum values could be recovered before the conversion of the niobium to ferroniobium. This problem has attracted the attention of interested laboratories, and, as a result, methods which include chlorine metallurgy and liquid-liquid separation are being investigated (19).

#### ANALYSIS

The analysis of tantalite-columbite ores has caused a great amount of concern among those interested in the use and proper evaluation of these ores (5,13,14). Mixtures of tantalum, niobium, and titanium do not give clear-cut reactions with reagents because the chemical behavior of one is modified by the presence of the others.

The oldest procedure for the separation of tantalum and niobium is the classical Marignac method, which takes advantage of the great difference in the solubilities of  $\text{K}_2\text{TaF}_7$  and  $\text{K}_2\text{NbOF}_6$  in water containing a little excess hydrofluoric acid. Modifications of this procedure are still used successfully for the analysis of tantalum ores. The modern version of this Marignac method, described below, uses the spectrograph to correct for the inaccuracies resulting from incomplete separation during crystallization. The important steps in this method are as follows:

(1) The earth acids (mixed tantalum and niobium pentoxides) are purified in the usual manner so that only the tantalum, niobium, and some of the titanium remain.

(2) The Marignac procedure is used to separate the earth acids into two fractions which are converted to oxides. One of these oxide fractions is  $\text{Ta}_2\text{O}_5$  containing  $\text{Cb}_2\text{O}_5$  and  $\text{TiO}_2$  as impurities, and the other is  $\text{Cb}_2\text{O}_5$  containing small amounts of  $\text{Ta}_2\text{O}_5$  and  $\text{TiO}_2$ .

(3) Corrections for the impurities present in the oxide fractions are made by quantitative spectrographic analyses of these fractions. Since the impurities are relatively small, the spectrographic corrections are quite accurate.

A procedure for the separation of tantalum from niobium, based on the fractional precipitation of their complexes with tannin (tannic acid, U.S.P. XIII), was published by Schoeller (13) after 17 years of work on these elements. This method has been

TABLE I. Tantalum Minerals.

Name	Composition	Ta <sub>2</sub> O <sub>5</sub> content, %	Color and luster	Sp. gr.	Mohs hardness	Crystal structure	Streak
Tantalite-columbite	(Fe,Mn)(Ta,Nb) <sub>2</sub> O <sub>6</sub>	0-86	Black, metallic	5.2-7.8	6-6½	Orthorhombic	Brown
Manganotantalite	Mn(Ta,Nb) <sub>2</sub> O <sub>6</sub>	40-82	Black, metallic	6.0-7.8	6-6½	Orthorhombic	Brown
Tapiolite	Fe(Ta,Nb) <sub>2</sub> O <sub>6</sub>	40-85	Black, metallic	6.0-7.8	6-6½	Tetragonal	Brown
Skogbolite	FeTa <sub>2</sub> O <sub>6</sub>	86	Black, metallic	7.8	6½	Tetragonal	Brown
Microcline	2CaO.Ta <sub>2</sub> O <sub>5</sub> + NbOF <sub>3</sub> as an impurity	60-70	Pale yellow to light brown, nonmetallic	5.2-6.2	5½	Isometric	Light gray
Simpsonite or calogerasite	Al <sub>2</sub> Ta <sub>2</sub> O <sub>8</sub> + CaO as an impurity	70-72	Cream to gray, nonmetallic	5.9-6.5	6½-7.0	Hexagonal	White to pale yellow
Thoreaulite	SnTa <sub>2</sub> O <sub>7</sub> + CaO and Nb <sub>2</sub> O <sub>5</sub> as impurities	60-75	White to light brown or gray, nonmetallic	7.6-7.9	6	Monoclinic	White to pale yellow
Stibiotantalite	(Sb,Bi)(Ta,Nb) <sub>2</sub> O <sub>6</sub>	35-60	Dark to light brown, resinous	5.5-7.5	5-7	Orthorhombic	Light yellow
Yttrotantalite	(Fe,Ca) <sub>2</sub> (Y,Er,Ce,U) <sub>2</sub> (Ta,Nb) <sub>2</sub> O <sub>15</sub> + 4H <sub>2</sub> O	30-45	Black, vitreous	5.5-6.8	5-5½	Orthorhombic	Gray to light brown
Tanteuxenite	(Y,Er,Ce,U)(Ta,Nb)(Ti) <sub>2</sub> O <sub>6</sub>	20-55	Black or brown, resinous	5.5-5.9	5½-6½	Orthorhombic	Gray to light brown

criticized for its large number of repetitive steps but, like the Marignac process, has been modified and is in regular use today (14).

The basis of the tannin separation is the differential solubility of the oxalotantallic and oxaloniobic acid complexes in the presence of tannin in a slightly acid solution. Tantalum is insoluble in the higher acid concentrations, while niobium precipitates only when less acid is present. Therefore, if the acidity is regulated by the careful addition of a base, the tantalum complex will come down first as a lemon-yellow precipitate followed by the niobium complex which is red. In typical manner, these reactions are not clear-cut, so a clean separation in one step is not possible. In one modification of the Schoeller method, the precipitation is regulated to produce a fraction which contains all the tantalum with small amounts of niobium and titanium. The niobium content of this tantalum fraction is determined volumetrically by reducing with zinc in sulfuric acid solution (niobium, but not tantalum, is reduced from valence 5 to 3) and titrating with permanganate. The titanium content is determined colorimetrically.

Recently, a procedure for the determination of tantalum in rocks and minerals has been developed by Dinnin (5). It is based on the tantalum-pyrogallol reaction recommended by Platanov and Krivoschikov and consists in measuring the absorbancy of the tantalum-pyrogallol complex at 325  $m\mu$  in 4 *N* hydrochloric acid and a fixed concentration (0.0175 *M*) of ammonium oxalate. This procedure is much simpler than any previously described, and, if it weathers the test of time, it will save many hours of analytical work in the evaluation of tantalum-bearing ores.

The possibility of using neutron activation techniques for the analysis of tantalum ores should not be overlooked. The sensitivity of detection for  $Ta^{182}$  has been estimated to be  $10^{-9}$  gram. This method should be especially suited for the examination of samples having low tantalum-to-niobium ratios and of those containing only small amounts of tantalum. Another recent approach to the analytical problem was made by Campbell and Carl (3), who have successfully applied x-ray fluorescent spectrography to the analysis of tantalum-niobium ores.

A rapid method for the approximate evaluation of tantalite-columbite minerals, based on the relationship of  $Ta_2O_5$  content to specific gravity, has been used for many years. A graph was obtained by plotting a great many analyses of clean minerals against their specific gravities; some figures from this curve are:

$Ta_2O_5$ , %.....	0	10	20	30	40	50	60	70	80
Sp.gr. of tantalite-columbite....	5.27	5.51	5.75	6.00	6.26	6.54	6.85	7.20	7.78

The results are surprisingly close to the ultimate analysis when clean pieces of tantalite-columbite mineral are used for specific gravity determinations. This method is very helpful in the preliminary examination of samples submitted by prospectors.

#### EXTRACTION AND METALLURGY

The production of pure ductile tantalum may be divided into four rather distinct steps: (1) the chemical extraction from the mineral concentrates, which yields a pure tantalum salt; (2) the reduction of the pure tantalum salt to metallic tantalum powder; (3) the compacting and sintering of the tantalum powder to produce a sound ductile bar; and (4) the working of the bar by rolling into sheet or drawing into wire and the fabrication of these products into useful articles.

**Chemical Extraction.** The mineral concentrates, which may contain 60% or more of  $(\text{Ta}, \text{Nb})_2\text{O}_5$  (at least 20%  $\text{Ta}_2\text{O}_5$ ), are pulverized and fused with sodium hydroxide. The resulting product is leached with water and treated with hydrochloric acid to produce a slurry of mixed tantalum and niobic acids. Most of the iron and manganese and some of the titanium are removed from the acid slurry by washing with water. The mixed earth acids are dissolved in hydrofluoric acid, and potassium fluoride is added in sufficient quantity to produce  $\text{K}_2\text{TaF}_7$  and  $\text{K}_2\text{NbOF}_6$ . Now, because of the difference in the solubilities of these complex fluorides, tantalum being less soluble, they may be separated and purified by crystallization.

**Reduction of Potassium Fluotantalate.** Potassium fluotantalate,  $\text{K}_2\text{TaF}_7$ , is the simplest tantalum compound to produce pure, and is the salt most commonly used in the preparation of tantalum powder. The reduction of this salt to metallic tantalum may be accomplished by the reaction at elevated temperatures with sodium or by the electrolysis of the fused salt in an iron or graphite pot.

In the sodium reduction process, a sealed iron vessel containing a mixture of the proper amounts of potassium fluotantalate and granular sodium is heated to initiate the exothermic reduction reaction. After cooling, the container is opened and the reaction product crushed and leached with water. The resulting powder is treated with acids to remove adhering impurities. The tantalum powder prepared by this method is very fine-grained and somewhat difficult to handle.

The reduction of potassium fluotantalate by electrolysis is the process used in the U.S. for the commercial production of tantalum powder. The fused salt, contained in an iron pot, is electrolyzed batchwise to produce a relatively coarse powder which is easily cleaned by washing with strong acids. The cell consists of an iron cathode and a carbon anode. Tantalum powder produced in this manner is soft and quite free from impurities which might be expected to make subsequent sintering difficult. A typical analysis of tantalum powder produced by electrolysis is: Ta, 99.8%; Fe, 0.016%; C, 0.12%; Nb, less than 0.01%; Ti, less than 0.05%.

**Processing by Powder Metallurgy.** The pure powder is compacted into bars in steel dies using a pressure of about 50 p.s.i. of punch surface. The pressed bar, which is strong enough to be handled carefully, is converted into a crystalline ingot by heating in a vacuum chamber in the range of 2100–2600°C. (several hundred degrees below the melting point of the metal). The bar is held between water-cooled terminals and is heated by its own resistance in an electric circuit. During this sintering process, certain residual impurities are vaporized and the resulting ductile bar may be forged and rolled into sheet or drawn into wire at room temperature. See *Powder metallurgy*.

**Production of Sheet, Wire, and Articles.** Tantalum metal is available as powder, sheet, wire, seamless tubing, and in fabricated shapes or welded assemblies. Wire is drawn as fine as 0.001 in. in diameter, and sheet (foil) is rolled to 0.0005 in. thick.

Sintered tantalum is about as ductile as annealed mild steel and ordinarily is worked at room temperature. When work hardening occurs, the metal is annealed in a vacuum at about 1200°C. It cannot be worked hot conveniently because it reacts with all common gases and becomes hard or brittle. It may be heated to redness only when protected by pure helium or argon. Tantalum sheet or rod may be welded if the metal is protected from exposure to the common gases while being heated. It may be seam-welded under water or arc-welded under carbon tetrachloride and responds very well to the newer inert-gas arc-welding process.

## PROPERTIES

**Physical Properties.** The physical properties of tantalum are given in Table II.

**Reactions.** Tantalum is completely inert in a great many chemicals (17), the important exceptions being the strong alkalis, fuming sulfuric acid (oleum), hydro-

TABLE II. Physical Properties of Tantalum.

Property	Value
M.p., °C.....	2996 ( $\pm 50^\circ$ )
Density, g./cu.cm., at 20°C.....	16.6
Lattice type.....	Body-centered cube
Lattice constant, Å.....	3.296
Vapor pressure, mm., at 1727°C.....	$9.5 \times 10^{-11}$
Sp.heat, cal./g., at 0°C.....	0.036
Linear coefficient of expansion, per °C.....	$6.5 \times 10^{-6}$
Thermal conductivity, cal./(sec.)(sq.cm.)(°C./cm.), at 20°C.....	0.130
Heat of combustion to Ta <sub>2</sub> O <sub>5</sub> , cal./g.....	1379
Tensile strength, p.s.i.	
Sheet, annealed, 0.010 in.....	50,000
Sheet, worked, 0.010 in.....	110,000
Wire, annealed, 0.002 in.....	100,000
Wire, worked, 0.002 in.....	180,000
Elongation, % in 2 in.	
Sheet, annealed, 0.010 in.....	40
Sheet, worked, 0.010 in.....	1
Wire, annealed, 0.002 in.....	11
Wire, worked, 0.002 in.....	1.5
Rockwell hardness, E scale	
Sheet, annealed, 0.010 in.....	60
Sheet, worked, 0.010 in.....	95
Young's modulus of elasticity, p.s.i.....	27,000,000
Directional properties, annealed sheet and worked sheet.....	The tensile strengths and elongations, measured parallel and transverse to rolling directions, are substantially equal in both worked and annealed sheet
Machinability index.....	Like cold-rolled steel with CCl <sub>4</sub> as lubricant
Coefficient of friction.....	Calls against itself and other metals
Electrical resistivity, microhms-cm.	
At 18°C.....	12.4
At 1000°C.....	54
At 1500°C.....	71
Temp. coeff. of electrical resistivity, per °C., at 0-100°C.....	0.00382
Work function, e.v.....	4.10
Positive ion emission, e.v.....	10.0
Electron emission, ma./sq.cm.	
At 2000°K.....	19.5
At 1500°K.....	$4.7 \times 10^{-3}$
At 1273°K.....	$1 \times 10^{-5}$

fluoric acid at any temperature, and concentrated sulfuric acid above 150°C. It is inert to most gases below 200°C. but absorbs hydrogen, and is embrittled, on dissolving slowly in dilute hydrofluoric acid, or cathodically in electrolysis.

When tantalum is heated in hydrogen above 250°C., it can absorb more than 700 volumes of this gas and become very brittle. The hydrogen can be removed by heating the brittle metal to about 1200°C. in vacuum. Tantalum is attacked by fluorine at room temperature, by chlorine at about 250°C., and by bromine at 300°C., but it is inert to iodine below a bright red heat. Tantalum is most readily dissolved in a mixture of hydrofluoric and nitric acids.

Tantalum powder reacts directly with carbon at high temperatures to form a carbide, TaC, and with boron to form TaB<sub>2</sub>. If a piece of fine tantalum wire is held in a Bunsen flame, it becomes incandescent and is rapidly converted to white tantalum oxide. Commercial tantalum metal powder is not pyrophoric.

Tantalum metal is an excellent electrolytic valve, that is, it passes current in only one direction when it is made an electrode in an acid electrolytic cell. This property plus its inertness to acid electrolytes has made it an important metal in the manufacture of current rectifiers and capacitors.

**Metallography.** The characteristic good ductility and poor machinability of tantalum make it difficult to prepare undistorted surfaces suitable for metallographic examination. The inertness of the metal to chemical attack has added to this problem. However, good photomicrographs are possible if patience and skill are practiced. The following procedure for metallographic surface preparation is in regular use: (1) the sample is mounted in plastic or in a tantalum holder; (2) wet-ground on 240-, 400-, and 600-grit paper; (3) polished on lap covered with dull side of slipper satin using diamond paste and kerosene; (4) polished on lap covered with "micro cloth" using No. 3  $\gamma$ -alumina; (5) etched in a solution of 10 ml. NH<sub>4</sub>OH + 10 ml. H<sub>2</sub>O + 20 ml. H<sub>2</sub>F<sub>2</sub> (48%) at 80°C.; and (6) repolished and re-etched until satisfactory surface is obtained.

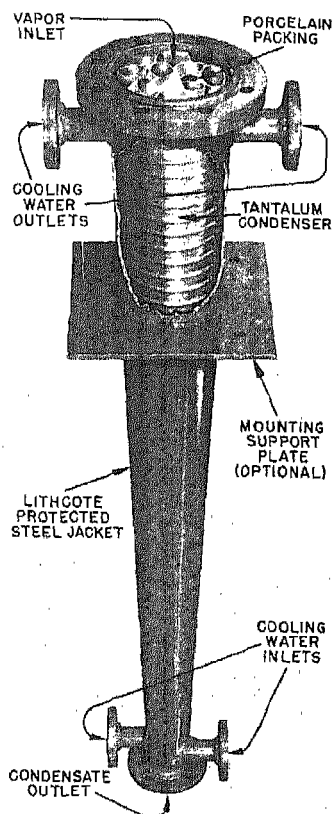
Excellent surfaces have been prepared by an electrolytic polishing and etching method using the following procedure (18): electrolyte: 90 ml. conc. H<sub>2</sub>SO<sub>4</sub>, 10 ml. 48% H<sub>2</sub>F<sub>2</sub>, at 40°C., with agitation. A platinum dish is used as the electrolyte container and cathode. The sample is electropolished for 9 min. at a current density of 0.10 amp./sq.cm. and then electroetched for 10 min. at a current density of 0.02 amp./sq.cm.

#### USES

The greater part of mined tantalum now finds its way into ferroniobium and ferrotantalum-niobium (these products are still usually known commercially as ferrocolumbium and ferrotantalum-columbium). However, the most important uses of tantalum are in the pure state (15). Commercial tantalum metal has a purity of 99.9+% (16). The largest single use of the pure metal is in the manufacture of acidproof equipment for the chemical processing industry, but the electronics industry absorbs almost as much. Probably the most rapidly increasing use is in the manufacture of electrolytic capacitors. The use of tantalum in surgery as suture wire and in bone repair is another application of increasing importance. Generally, the unique properties of the metal and its relatively high cost determine the scope of its use. See also under "Alloys" and under "Compounds."

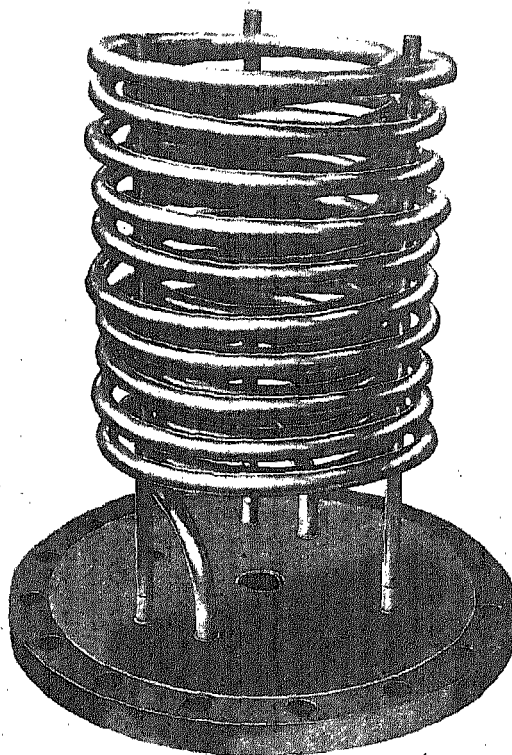
**Acidproof Chemical Processing Equipment.** Tantalum has been used in the fabrication of chemical processing equipment since about 1930. Its remarkable corrosion resistance, weldability, ductility, and good strength make it well suited for the fabrication of equipment used for handling highly corrosive chemicals. See

Vol. 7, p. 665. The advantages offered by inertness to acid chemicals, high heat transfer, and tolerance to extreme temperature changes outweigh the higher first cost of tantalum equipment. Reactors, vapor condensers, bayonet heaters, and large multi-tube heat exchangers are made from tantalum sheet only 0.013–0.020 in. thick. This thin-wall construction, which permits high heat transfer efficiency, is possible because of the high strength and complete inertness of the metal. Industrial equipment



*Courtesy Fansteel Metallurgical Corp.*

**Fig. 1. Tantalum condenser.** The tapered shape provides for good contact of vapor with the condenser wall as the volume decreases.



*Courtesy Fansteel Metallurgical Corp.*

**Fig. 2. Tantalum coil.** Additional heating capacity is obtained by building the coil on a large steel flange protected by a tantalum sheet. The flange is mounted at the bottom of the kettle or tank.

varies in size from miniature thermometer wells to a large multitube boiler consisting of 182 seamless tantalum tubes,  $\frac{3}{4}$  in. in diameter by 5 ft. long. Such a unit is capable of transmitting 4 million B.t.u. per hour using 150 lb. steam. See Figures 1 and 2.

**Vacuum Tubes (q.v.).** The first vacuum tube using tantalum in its construction was made in 1927. Since that time, tantalum has become an important component in certain types of power tubes because of a combination of properties that are useful in the fabrication of these tubes. First, the metal is easily formed and welded into the shapes required. Second, its resistance to corrosion makes chemical cleaning of components with strong, hot acids possible. Third, excellent hot strength and low

vapor pressure make possible rapid high temperature degassing of the tube. Fourth, tantalum acts as a "getter" in the completed tube because it effectively absorbs and holds residual gases when heated to temperatures between 700 and 1200°C.

**Electrolytic Capacitors and Rectifiers.** The tantalum industry in the U.S. began in 1922 with the manufacture of the Balkite battery charger, which used tantalum as the rectifying electrode in an electrolytic cell. Although this use has long since been largely replaced by other devices for current rectification, it was the forerunner of a rapidly increasing application, the tantalum capacitor.

The tantalum capacitor itself is not new, but its greatest development has occurred since the late 1940's. The demand for miniature capacitors, for use in voice or signal transmission, radar, and other electronic devices, has resulted in extensive investigations of materials suitable for the construction of these units. Tantalum is well suited in many ways for this application. For example, it is resistant to many corrosive electrolytes and forms a stable, thin electrolytic oxide film whose dielectric constant, 11.5, is about 50% higher than that of aluminum.

Two types of construction are used in the manufacture of tantalum capacitors, the conventional foil assembly and an entirely new principle using a porous tantalum electrode in a silver container. The foil-type capacitor is composed of two 0.0005-in. tantalum ribbons separated by a porous ribbon of insulating material saturated with a glycol-base electrolyte. These ribbons are rolled into a cylinder and sealed in a metal container. Such a capacitor has excellent stability and has a lower temperature coefficient than that of aluminum cells. It occupies about one-seventh of the space required for an aluminum foil paper unit of equivalent capacitance at 100 volts. In the sintered porous capacitor the anode is made by pressing tantalum powder around a tantalum wire core and sintering this compact at a temperature that will weld the particles of powder together but still allow the anode to remain porous. This results in an anode with a relatively large active-surface-to-weight ratio. A silver can which is used as the cathode is crimp-sealed around the anode, using an insulating separator. The porous tantalum capacitor has a very high capacitance-to-size ratio. A typical unit  $\frac{3}{8}$  in. in diameter and  $\frac{3}{4}$  in. in length is rated at 50 microfarads at 60 working volts d.c.

The advantages of tantalum capacitors are greater service life, better idle life, wider temperature range, and higher capacitance-to-size ratio.

**Surgical Applications** (see *Surgical sutures*). One of the earliest applications of tantalum was the fabrication of surgical and dental instruments, but its uses in modern surgery, although very important, do not include these articles. Because tantalum does not react with body fluids and is tolerated by animal tissue, it has become an important metal in the manufacture of suture wire and bone repair plates. Also, mesh woven from tantalum wire is used to support weakened muscles in repairs to the abdominal wall.

**Miscellaneous Uses.** Other uses for pure tantalum include spinnerets for the production of synthetic fibers, extrusion rings used in the manufacture of synthetic sausage casings, electroplating anode baskets, and laboratory ware.

#### ALLOYS

Tantalum forms alloys with iron, nickel, cobalt, chromium, niobium, tungsten, zirconium, and many others, but does not alloy with such metals as copper, zinc, calcium, and mercury. It forms the compound  $\text{Al}_3\text{Ta}$  with aluminum. All the alloys



of tantalum are less resistant to corrosion than the pure metal, and none is used as a substitute for this purpose.

The most important alloys of tantalum are ferrotantalum-niobium and ferro-niobium. The close association of tantalum and niobium in their ores is largely responsible for the presence of tantalum in these alloys; the ores are converted to ferroalloys by direct reduction in an electric furnace.

The ferroalloys are used to inhibit intergranular deterioration in austenitic stainless steels. They are added in sufficient quantity to assure the formation of tantalum and niobium carbides with the small amount of carbon remaining in this type of steel. Ferrotantalum is not so efficient as ferroniobium in this application because, since tantalum has twice the atomic weight of niobium, a given weight combines with less carbon. The ferroalloys are used also in the manufacture of 4-6% chromium steels to inhibit air hardening and as an alloying component in certain special-purpose steels. Ferrotantalum-niobium contains about 20% tantalum, and ferroniobium contains about 6% tantalum.

#### ECONOMIC ASPECTS

In 1954, high-grade tantalite, 60%  $Ta_2O_5$ , was traded at \$8.00 per pound of contained  $Ta_2O_5$ . The base price in 1954 for tantalum sheet (0.065-0.100 in.) was \$44.50 per pound. In September 1954, ferroniobium sold for \$12.00 per pound of contained Nb, and ferrotantalum-niobium sold for \$6.25 per pound of contained Ta and Nb.

#### Tantalum Compounds

The refractory nature of tantalum prevents the formation of many ordinary simple compounds of this element. Of those that have been prepared, only a very few may be considered important.

Tantalum carbide,  $TaC$ , is an important compound used, in combination with tungsten carbide,  $WC$ , and cobalt, in the manufacture of hard carbide cutting tools and wear-resisting parts. This carbide has the effect of reducing the coefficient of friction of the tool, thereby depressing the tendency of the chips to weld to the cutting face. Tools containing tantalum carbide are used extensively for the machining of steels. See also *Carbides (heavy-metal)*.

Potassium fluotantalate,  $K_2TaF_7$ , is used in the preparation of a catalyst which is used in the synthesis of butadiene from alcohol. Tantalum oxide,  $Ta_2O_5$ , is used in the manufacture of a special optical glass for aerial camera lenses.

#### Aluminum Tantalide.

Aluminum tantalide,  $Al_3Ta$ , formula weight 261.89, sp.gr. 7.02, is a gray refractory powder which forms when aluminum metal is added to potassium fluotantalate at about 1000°C. It is quite insoluble in acids and alkalis. It oxidizes very slowly when heated in air above 500°C. It melts in a vacuum at about 1400°C. when it begins to lose some aluminum.

**Tantallic Acid, Tantalates.** See "Tantalum oxides and tantallic acid."

#### Tantalum Boride.

Tantalum boride,  $TaB_2$ , formula weight 202.59, sp.gr. 12.38, m.p. about 3000°C. Mohs hardness 9+, is a gray metallic powder. It is quite insoluble in acids and al-

kalies. It may be prepared by heating tantalum and boron in a vacuum at about 1800°C., by induction-heating a mixture of  $Ta_2O_5$ ,  $B_2O_3$ , and C, or by the electrolysis of fused  $Ta_2O_5$ ,  $B_2O_3$ , CaO, and  $CaF_2$  (10).

**Tantalum Bromide.** See "Tantalum halides."

#### Tantalum Carbide.

Tantalum carbide, TaC, formula weight 192.96, sp.gr. 14.65, m.p., 3880°C., is a crystalline brown powder. It is insoluble in all acids except a mixture of hydrofluoric and nitric acids. Its Mohs hardness is between 9 and 10. It is an interstitial compound with a face-centered cubic lattice. Stoichiometric tantalum carbide may be prepared by the direct carburization of tantalum powder with the appropriate amount of lampblack, or by the reaction of tantalum oxide and lampblack at about 1900°C. in an inert atmosphere. The valency of tantalum does not determine the stoichiometric composition of the carbide. Tantalum carbide is converted to the pentoxide when heated to redness in air. It is easily decomposed for analytical purposes by fusion with potassium pyrosulfate or by solution in a mixture of hydrofluoric and nitric acids.

Tantalum carbide with a hexagonal structure has also been reported (6).

#### Tantalum Halides.

**Tantalum pentachloride**,  $TaCl_5$ , formula weight 358.24, sp.gr. 3.68, m.p. 220.0°C. b.p. 239.3°C., is a white (when pure) crystalline salt which hydrolyzes in water but is soluble in absolute alcohol. It hydrolyzes on exposure to moist air. It is formed when tantalum metal is heated in pure dry chlorine above 200°C. It may also be prepared by heating a mixture of tantalum pentoxide and carbon in pure dry chlorine. It decomposes to tantalum and hydrogen chloride when heated above 600°C. in hydrogen.

**Tantalum oxytrichloride**,  $TaOCl_3$ , formula weight 303.32, is a crystalline salt that forms, with some pentachloride, when tantalum pentachloride is distilled in dry air. It hydrolyzes in water.

**Tantalum tribromide**,  $TaBr_3$ , formula weight 239.75, is formed when the pentabromide is reduced with hydrogen at 700°C. (19). It reacts with water and alkali liberating hydrogen and forming  $TaO_2 \cdot 2H_2O$ .

**Tantalum pentabromide**,  $TaBr_5$ , formula weight 580.53, sp.gr. 4.67, m.p. 280°C., b.p. 348.8°C., is a yellow crystalline salt which hydrolyzes in water. It can be prepared by heating tantalum metal in pure bromine gas above 300°C. Vapor pressures of the liquid have been reported (1).

**Tantalum pentaiodide**,  $TaI_5$ , formula weight 715.50, m.p. 496°C., b.p. 543°C., forms as shiny black crystals when tantalum metal is heated to a bright red heat in iodine. It hydrolyzes when exposed to air but does not decompose below its boiling point when protected. It loses iodine when heated somewhat above 1000°C. (1). Vapor pressures of the liquid have been reported (1).

**Tantalum pentafluoride**,  $TaF_5$ , formula weight 275.95, sp.gr. 4.74, m.p. 96.8, b.p. 229.5, is a colorless crystalline salt which is soluble in water without hydrolysis. It may be prepared conveniently by reacting anhydrous hydrogen fluoride with

tantalum pentachloride at room temperature. It is formed also when tantalum metal is heated in a stream of fluorine.

Tantalum forms a number of double fluorides of which potassium fluotantalate is the best known.

**Potassium fluotantalate (potassium tantalum fluoride)**,  $K_2TaF_7$ , formula weight 392.15, sp.gr. 5.24, m.p.  $720^\circ \pm 10^\circ C.$ , crystallizes as colorless rhombic needles when potassium fluoride is added to a solution of tantalum fluoride with an excess of hydrofluoric acid. It hydrolyzes when boiled in water containing no free hydrofluoric acid. Its solubility in acidulated water varies from 60 g./100 ml. boiling to less than 0.5 g./100 ml. cold. The difference in solubility characteristics of  $K_2TaF_7$  and  $K_2NbOF_5$  is used in the industrial separation of tantalum from niobium. Potassium fluotantalate was produced first by Berzelius in 1825 and is the most important salt of tantalum today.

Tantalum fluoride forms complexes with the fluorides of the alkali metals, the alkaline earth metals, certain heavy metals, ammonia, and pyridine. C. W. Balke (2) investigated and described the following:  $2NH_4F.TaF_5$ ,  $3NaF.TaF_5$ ,  $2NaF.TaF_5.H_2O$ ,  $2RbF.TaF_5$ ,  $ZnF_2.TaF_5.7H_2O$ ,  $CuF_2.TaF_5.4H_2O$ ,  $LiF.TaF_5.2H_2O$ ,  $NaF.TaF_5$ ,  $CsF.TaF_5$ ,  $2CsF.TaF_5$ ,  $C_6H_5N.HF.TaF_5$ , and  $3(C_6H_5N.HF).TaF_5.2H_2O$ . An oxy-fluoride complex,  $2KF.TaO_2F_3.H_2O$ , was also found.

### Tantalum Hydride.

Tantalum hydride,  $TaH$ , formula weight 181.95, sp.gr. 15.1, is a gray brittle material with a metallic luster. Tantalum metal absorbs hydrogen by cathodic electrolysis or when heated in hydrogen at a red temperature. Hydrogen is absorbed to the extent of  $TaH_{0.76}$  or about 740 volumes (8). The absorption is accompanied by an expansion of the body-centered crystal lattice and by an increase in molecular volume of the tantalum. The absorbed hydrogen is liberated when the hydride is heated to  $1200^\circ C.$  and cooled in a vacuum. Tantalum hydride exhibits superconductivity at low temperatures (7). It resists attack by acids.

### Tantalum Nitride.

Tantalum nitride,  $TaN$ , formula weight 194.96, sp.gr. 16.30, m.p.  $3090^\circ C.$ , forms in hexagonal dull gray crystals when tantalum is heated in pure nitrogen at about  $1100^\circ C.$  Nitrogen is liberated if the nitride is heated to  $2000^\circ C.$  and cooled in a vacuum. Tantalum nitride is insoluble in acids but is easily decomposed by potassium hydroxide with the evolution of ammonia. It is an interstitial compound, like the carbide. It does not exhibit superconductivity above  $1.88^\circ K.$  (7).

### Tantalum Oxides and Tantallic Acid.

**Tantalum(II) oxide** is not easily prepared, but its existence has been reported. Tantalum tribromide decomposes in water to a brown powder,  $TaO_2.2H_2O$ , which changes to the pentoxide in air at room temperature (20). An impure  $Ta_2O_4$  is probably formed when the pentoxide is partially reduced with carbon at  $1900^\circ C.$

**Tantalum pentoxide, tantalum oxide**,  $Ta_2O_5$ , formula weight 441.90, sp.gr. 8.735, m.p.  $1470^\circ C.$ , is a rhombic white powder, insoluble in water and in most acids and alkalies. It reacts slowly with hot hydrofluoric acid. It can be taken up by fusion

with potassium pyrosulfate or alkali-metal hydroxides or carbonates. It is prepared by the ignition in air of tantalum metal, tantalum hydride, or tantalum carbide or by heating tantalic acid. Tantalum oxide reacts with carbon at 1900°C. to form the carbide and with sulfur monochloride at a dull red heat to form the pentachloride.

**Tantallic acid**,  $\text{HTaO}_3$ , or probably more correctly  $\text{Ta}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ , is the name given to hydrated forms of tantalum oxide. It is a white insoluble precipitate which forms when (1) a potassium pyrosulfate fusion containing tantalum is leached with water, (2) a solution of tantalum fluoride is made ammoniacal, (3) a solution of alkali tantalates is acidulated with hydrochloric acid, or when (4) a halide of tantalum is hydrolyzed by boiling in water.

Tantallic acid forms organic complexes with tannic, oxalic, tartaric, salicylic, citric, and pyrogallic acids. These complexes are very useful to the analytical chemist. The following are the most important:

(1) When tantalic acid is formed in the presence of a tannin, a voluminous characteristic yellow precipitate, which is completely insoluble in water or dilute hydrochloric acid, is produced.

(2) On the other hand, the oxalic and tartaric complexes of tantalic acid are soluble in water.

(3) The pyrogallol-tantallic acid complex is colored, so it is used in the spectrophotometric determination of tantalum (5).

Tantallic acid is very weakly acidic; it readily reacts and dissolves with either hydrofluoric acid or potassium hydroxide. When tantalic acid is ignited, tantalum pentoxide is formed.

Tantallic acid forms several series of tantalates. Some of these occur in nature (see Table I) and many others have been prepared in the laboratory (9).

**Potassium tantalate or orthohexatantalate** (4:3 ratio),  $4\text{K}_2\text{O} \cdot 3\text{Ta}_2\text{O}_5 \cdot 16\text{H}_2\text{O}$ , formula weight 1990.5, is a colorless monoclinic salt which is soluble in water. It is the most common potassium salt of tantalum and is prepared by dissolving a fusion of potassium hydroxide and tantalum pentoxide in water and crystallizing the salt by evaporation. Cesium and rubidium form tantalates in this series which carry only 14 molecules of water.

**Potassium metatantalate** (1:1 ratio),  $\text{K}_2\text{O} \cdot \text{Ta}_2\text{O}_5$ , formula weight 635.1, is a white insoluble salt prepared by leaching calcined potassium hexatantalate with water.

**Potassium pertantalate**,  $\text{K}_3\text{TaO}_8$ , formula weight 426.25, is a white anhydrous salt which forms when tantalic acid is dissolved in a solution of potassium hydroxide and hydrogen peroxide. It decomposes with the evolution of oxygen when placed in boiling water. When treated with dilute sulfuric acid, a white precipitate, **metapertantallic acid**,  $\text{HTaO}_4 \cdot n\text{H}_2\text{O}$ , is formed.

**Sodium orthohexatantalate** (4:3 ratio),  $4\text{Na}_2\text{O} \cdot 3\text{Ta}_2\text{O}_5 \cdot 25\text{H}_2\text{O}$ , formula weight 2023.68, is the white insoluble compound which is formed when a fusion of tantalum pentoxide and sodium hydroxide is leached with water. It is slightly soluble in water but insoluble in solutions of sodium hydroxide or sodium chloride. It is converted to tantalic acid when treated with hydrochloric acid.

**Sodium pentatantalate** (7:5 ratio),  $7\text{Na}_2\text{O} \cdot 5\text{Ta}_2\text{O}_5 \cdot 24\text{H}_2\text{O}$ , formula weight 3075.46, is similar to the orthohexatantalate. It is formed when sodium hydroxide is added to an aqueous solution of potassium tantalate or potassium fluotantalate.

**Sodium metatantalate** (1:1 ratio),  $\text{Na}_2\text{O} \cdot \text{Ta}_2\text{O}_5 \cdot 2\text{H}_2\text{O}$ , formula weight 521.89, is obtained when the orthohexatantalate is calcined and then extracted with water to

remove the free alkali. It is a white insoluble material which, like the other sodium tantalates, is converted to tantalic acid when treated with hydrochloric acid.

**Sodium metapertantalate**,  $\text{NaTaO}_4 \cdot \text{NaTaO}_5 \cdot 13\text{H}_2\text{O}$ , and **sodium orthopertantalate**,  $\text{Na}_3\text{TaO}_8 \cdot \text{H}_2\text{O}$ , were prepared by Melikoff and Pissarjewsky (9) and are described as white amorphous powders, sparingly soluble in water, whose solutions liberate oxygen when heated. The per-salts are produced by the addition of hydrogen peroxide to solutions of the tantalates.

### Tantalum Sulfide.

Tantalum sulfide,  $\text{Ta}_2\text{S}_4$ , formula weight 490.16, is a black crystalline powder which is stable below  $1300^\circ\text{C}$ . It is insoluble in water and very slowly attacked by hydrofluoric, sulfuric, and nitric acids. It is decomposed by fusion in potassium hydroxide or pyrosulfate. It is formed by heating tantalum metal to a red heat in sulfur vapor.

### Bibliography

- (1) Alexander, K. M., and Fairbrother, F., *J. Chem. Soc.*, **1949**, S223.
- (2) Balke, C. W., *J. Am. Chem. Soc.*, **27**, 1140 (1905).
- (3) Campbell, W. J., and Carl, F., *Anal. Chem.*, **26**, 800 (1954).
- (4) *Columbium-Tantalum Purchase Program*, Defense Procurement Agency, 1952, ch. 23.
- (5) Dinnin, J. I., *Anal. Chem.*, **25**, No. 12, 1803 (1953).
- (6) Ellinger, F. H., *Trans. Am. Soc. Metals*, **31**, 89 (1943).
- (7) Horn, F., and Zweigler, W., *J. Am. Chem. Soc.*, **69**, 2762 (1947).
- (8) Hurd, D., *Chemistry of the Hydrides*, Wiley, N.Y., 1952.
- (9) Mellor, 1929, Vol. IX, p. 883.
- (10) Norton, J. T., Blumenthal, H., and Sindeband, S. J., *J. Metals*, **1**, No. 10, 749 (1949).
- (11) Palache, Berman, and Frondel, 1944-.
- (12) Parsons, A. B., *J. Franklin Inst.*, **239**, No. 6, 437 (1945).
- (13) Schoeller, W. R., *The Analytical Chemistry of Tantalum and Niobium*, Chapman & Hall, London, 1937.
- (14) Slavin, M., and Pinto, C., *A Tania do Nordeste Sua Exportação e Análise* (Bol. 21), Ministeria da Agricultura, Brazil, 1946.
- (15) Taylor, D. F., "Tantalum and Columbium," in *Modern Uses of Nonferrous Metals*, Am. Inst. Mining Met. Engrs., N.Y., 1953, p. 395.
- (16) *The Metal Tantalum*, Fansteel Metallurgical Corp., North Chicago, Ill., 1953.
- (17) Uhlig, H. H., *The Corrosion Handbook*, Wiley, N.Y., 1948.
- (18) Wensch, G., Bruckart, K., and Conolly, M., *Metal Progress*, **61**, No. 3, 81 (1952).
- (19) Werning, J. R., Higbie, K. B., Grace, J. T., Speece, B. F., and Gilbert, H. L., *Ind. Eng. Chem.*, **46**, No. 4, 644 (1954).
- (20) Young, R., and Hastings, T., *J. Am. Chem. Soc.*, **64**, No. 7, 1740 (1942).

D. F. TAYLOR

**TAPIOCA.** See *Starch*, Vol. 12, p. 772.

**TAR ACIDS.** See *Cresol*, Vol. 4, p. 602; *Phenol and phenols*, Vol. 10, p. 282; *Tar and pitch*.

**TAR AND PITCH**

The term tar is applied to a wide variety of brown to black viscous liquids produced in connection with the destructive distillation of such organic materials as coal, petroleum, and wood. Similarly, the term pitch is applied to residual products resulting from the distillation of each variety of tar.

This article will deal principally with tars produced by the destructive distillation, or carbonization, of coal, and to a minor extent with water-gas and oil-gas tars derived from petroleum distillates or residuals when the latter are cracked or gasified for the production of manufactured gas. See also *Asphalt*; *Carbonization*; *Coal*; *Hydrogenation*; *Manufactured gas*.

Generally speaking, tars produced by the destructive distillation or carbonization of coal contain major quantities of hydrocarbons and minor amounts of oxygen, nitrogen, and sulfur-bearing compounds. They also contain minor quantities of dispersed, finely divided, carbonaceous materials and mineral matter. In each of these respects except color, coal tars may differ widely from one another, depending upon the coals from which they are produced, the temperatures at or to which the coals are carbonized, and the extent to which the tars are subjected to cracking or pyrolyzing conditions after their initial distillation from the coal particles.

Although coal tar had been distilled at a much earlier period, the commercial distillation of coal to obtain gas, coke, and tar began near the end of the 18th century in England. The coal was carbonized in small, cast-iron retorts which were heated to relatively low temperatures. The coke was used in iron foundries, the gas for lighting, and for a time the tar was used in shipbuilding.

The increased use of coal gas for illuminating purposes in London and other British cities in the early part of the 19th century resulted in the production of larger quantities of tar for which there were no adequate markets. However, the gradual development of commercial uses, such as the preservative treatment of wood with coal-tar creosote, the construction of tar roads, the briquetting of coal fines with coal-tar pitch, and the production of dyes from coal-tar chemicals, led to the establishment of tar distillation as a separate industry, particularly in England, Germany, and the U.S.

In each of these countries the production of coal tar followed a somewhat similar pattern. The original horizontal, cast-iron retorts were soon superseded by horizontal, refractory retorts which had greater capacities and permitted the coal to be carbonized at higher temperatures for the production of illuminating gas. The introduction of coke ovens for metallurgical coke production, following their development in France by Knob and by Carvés, further expanded coal-tar production and stimulated the growth of the coal-tar distilling industry, particularly in Germany, during the latter part of the 19th century.

Each of these changes in carbonizing equipment was accompanied by changes in the physical and chemical characteristics of the tars and products derived therefrom. Further changes accompanied the introduction, during the early part of this century, of vertical retorts and also coke ovens for manufactured-gas production. Other changes are now taking place as a result of the development of improved methods for the carbonization of coal at low temperatures.

In general, it may be said that four types of coal tar are produced in each of the principal tar-producing countries: coke-oven tar, vertical-retort tar, horizontal-retort tar, and low-temperature tar. However, the proportions of the various types of tar differ widely in the various countries. In 1952 approximately 99.2% of all coal tar produced in the U.S. came from coke ovens; about 0.7% from low-temperature retorts; and 0.1% from horizontal and vertical retorts. In Great Britain horizontal and vertical retorts are still used extensively for gas-making purposes with the result that a large proportion of the total coal tar comes from those sources. The proportion of low-temperature tar in Great Britain is small but somewhat larger than in the U.S. In Germany the proportion of low-temperature tar is greater than that of

the other countries, and high-temperature tar comes principally from coke ovens that have largely replaced horizontal and vertical retorts as in the U.S.

### Production

**U.S. Production.** Coal-tar production in the U.S. is given in Table I. In 1912 the 55,000,000 gallons of vertical and horizontal retort tars was converted principally into creosote for wood preservation, refined tars for the construction and maintenance of roads, and pitches for roofing and coal-briquetting purposes. The 110,000,000 gallons of coke-oven tar produced at steel plants for the most part was used as fuel for open hearth furnaces.

TABLE I. U.S. Coal-Tar Production.  
(Millions of Gallons.)

Year	Coke ovens	Vertical and horizontal retorts	Low-temperature retorts	Total
1912	110.0	55.0	—	165.0
1920	360.6	51.2	—	411.8
1930	602.5	42.0	—	644.5
1935	450.3	—	—	—
1940	673.3	22.0	—	695.3
1945	696.3	19.8	3.2	719.3
1950	739.9	4.4	4.9	749.2
1951	795.3	2.9	4.9	803.1
1952	703.9	0.9	4.9	709.7
1953	828.7	—	4.6 <sup>a</sup>	833.4

<sup>a</sup> Includes vertical- and horizontal-retort tars.

After the outbreak of World War I, hundreds of additional coke ovens were installed to supply the needs of the rapidly expanding metallurgical industries for coke, and also at gas plants instead of horizontal and vertical retorts. After a decline between 1929 and 1933 coke-oven tar again increased with some fluctuations to a maximum of 828,000,000 gallons in 1953.

**World Production.** According to statistics published in Great Britain (19), total coal-tar production by seventeen countries in 1951 was approximately 2,149,000,000 gallons. Of this amount the U.S. produced about 795,000,000 gallons (37%); Great Britain about 632,000,000 (29%); Germany about 323,000,000 (15%); and France approximately 124,000,000 (6%). The total production of these four countries was, therefore, about 1,874,000,000 gallons, or approximately 87% of the total reported for the seventeen countries.

**Distribution of U.S. Coal-Tar Production.** In the early days of coke-oven tar production in the U.S. most of the crude coke-oven tar produced at steel plants was used as fuel for open hearth furnaces and boilers. However, as markets for coal-tar products were developed, the burning of crude tar by the producers diminished and the tar thus released was sold to commercial tar-distilling companies. By 1924 the proportion of the crude tar burned by producers had been reduced to about 50%.

Shortly thereafter some of the producers began to partially distill or top their tars in order to obtain chemical oils for their own use or for sale to others. The soft pitches made by such topping operations were then used as open hearth and boiler fuels instead of crude tars. By 1929 about 43,000,000 gallons or 6.3% of the total

coke-oven tar production was being processed in this manner. Since that time other producers have undertaken the topping of their tars. As shown by Table II, the proportion of the total tar distilled by producers during the period from 1944 to 1953 averaged about 27%.

TABLE II. Distribution of Total U.S. Coal-Tar Production.

Year	Total tar, million gallons	Sold or consumed as fuel		Distilled or topped by producers		Distilled or used by others than producers	
		Million gallons	% of total	Million gallons	% of total	Million gallons	% of total
1944	791	173	21.9	201	25.4	417	52.7
1946	618	76	12.3	155	25.2	385	62.5
1948	753	172	22.8	194	25.8	387	51.4
1950	749	129	17.3	203	27.1	417	55.6
1951	803	123	15.3	252	31.4	428	53.3
1952	710	115	16.2	220	31.0	375	52.8
1953	833	144	17.3	254	30.5	435	52.2

### Properties

The characteristics of coal tar produced in different countries depend principally on the types of carbonizing equipment employed. In the U.S. in 1953 more than 99% of all coal tar produced came from chemical recovery coke ovens charged with bituminous coal. The physical and chemical characteristics of the tars produced at 32 coke-oven plants in 1952 are listed in Table III.

TABLE III. Characteristics of Coal Tars Produced in 32 U.S. Coke Plants in 1952.

Characteristic	Minimum	Maximum	Average
$d_{15.5}^{15.5}$	1.158	1.240	1.198
Benzene-toluene insoluble, % by wt.	2.32	14.50	7.84
Specific viscosity, Engler, 50°C.	6.0	110.0	29.0
Distillation % by wt.			
To 170°C.	2.3	12.0	7.3
To 270°C.	9.4	20.4	15.6
To 300°C.	14.6	26.7	21.5
To 355°C.	26.4	43.2	35.8
Softening point, °C. (ring and ball) of residue (see Vol. 2, p. 173)			
At 300°C.	35.2	53.2	44.2
At 355°C.	64.2	96.7	74.5
Tar acids, % of dry tar, by wt.	0.38	3.24	1.53
Tar bases, % of dry tar, by wt.	0.58	1.06	0.80
Naphthalene, % of dry tar, by wt.	6.7	12.2	9.6

British coal tars differ more widely in their characteristics, since there are four major sources of tar: coke ovens, horizontal retorts, intermittent vertical retorts, and continuous vertical retorts. Typical analyses of each have been published by Forsdike (14). Additional analyses of British tars, including low-temperature coal tar from one producer, have been presented by Coulson and Jones (7).

German high-temperature coal tars come principally from chemical recovery ovens and are similar to coke-oven tars produced in the U.S. However, German low-



temperature tars, unlike those made in England and the U.S., come principally from brown coal, carbonized in Lurgi-Spülgas retorts.

**Effect of Temperature.** The factor which has the greatest effect on coal-tar yields and characteristics is carbonizing temperature. Experimental results reported by Fieldner and Davis (11) showed that the yield of coal tar decreased from 18.2 gal. per ton or 7.6% by weight to 7.1 gal. per ton or 3.6% by weight when one bituminous coal (Pratt) was carbonized at 100-degree intervals from 900 to 1100°C. (932–2012°F.) in a series of tests in which all conditions were the same except the carbonizing temperature.

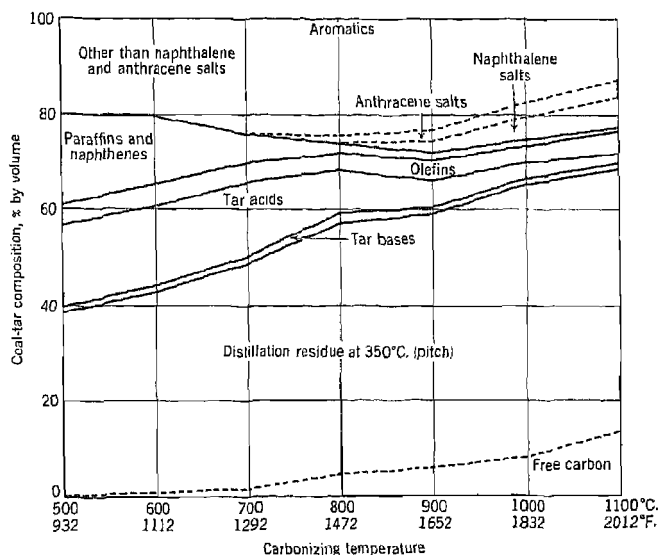


Fig. 1. Changes in the composition of coal tar with changes in carbonizing temperature.

The changes in the composition of the coal tar that occurred each time that the carbonizing temperature was raised 100 centigrade degrees are shown by the curves in Figure 1. The significance of the changes has been discussed by Fieldner and Davis (11), by Fisher (13), and by Rhodes (33). The following general observations were made by Fieldner and Davis: "With increasing carbonizing temperature the pitch content of the tar is increased at the expense of the more volatile constituents; in harmony with this trend the free carbon and the specific gravity of the tar increase, while neutral oils and tar acids decrease. The aromatic constituents, being relatively stable at high temperatures, increase with carbonizing temperature and the paraffins, being less stable, decrease. The percentage of olefins does not vary greatly with carbonizing temperature. It must be emphasized that these are relative trends. The yields per ton of coal of these constituents, except the pitch, decrease as the carbonizing temperature is raised, since the total yield of tar declines rapidly as the carbonizing temperature is raised."

Carbonizing temperatures usually are designated as low, mid or medium, and high. According to Fisher (13), Fieldner has set the temperature limits of low- and high-temperature carbonization at 450–700°C. (842–1232°F.) and 900–1200°C. (1652–2192°F.) respectively. This classification leaves the range 700–900°C. (1232–

1652°F.) for mid-temperature carbonization. On the basis of tar compositions, the curves in Figure 1 indicate that more appropriate temperature ranges might be as follows: below 600°C. (1080°F.) for low-temperature carbonization, 600–800°C. (1080–1472°F.) for mid-temperature carbonization, and 800–1200°C. (1472–2192°F.) for high-temperature carbonization, since the more abrupt and most significant changes in tar composition appear to take place at 600°C. (1080°F.) and 800°C. (1472°F.) respectively. However, the interval 600–700°C. (1080–1292°F.) is generally accepted as belonging in the low-temperature range, even though operation at temperatures above 600°C. requires the use of refractory retorts, which usually are associated with mid- or high-temperature carbonizing operations.

**Effect of Other Factors.** The assignment of temperature ranges in the three tar classifications mentioned above is further complicated by the fact that factors other than carbonizing temperature influence tar compositions and characteristics, although to a lesser extent. Especially important in this connection is the type of equipment and its method of operation. Various types of carbonizing equipment and their methods of operation have been described by Denig (10), Gluud and Jacobson (18), Keeling and Jung (23), Rhodes (33), Porter (30), and others.

"The main decomposition of coal," according to Vahrman (37), "sets in at about 300°C. (572°F.)." In this same connection Hansen (21) has observed that "coal begins to give off bitumen at about 300°C., a process which is completed at about 500°C. Upon further heating, the residual coke gives off gases only."

The tar released at this initial decomposition point would rightly be called primary tar if it could be recovered without further alterations resulting from secondary decompositions. It is unlikely that true primary coal tar, completely unaffected by secondary decompositions, has been recovered and analyzed, but it is probable that coal tar produced by Juettner and Howard (22) approached it closely in chemical composition and physical characteristics. They distilled the coal under conditions approaching molecular distillation by heating it to 525°C. (981°F.) at less than 0.01 mm. pressure of mercury. As summarized by Vahrman, "The tar was viscous and contained brown, amorphous solids, designated as 'bitumens' which were insoluble in light petroleum and diethyl ether . . . These amorphous solids could not be redistilled even in a molecular still, without the formation of phenols, gaseous and liquid hydrocarbons, bitumens, and coke residue. They appeared to be a primary, thermal, decomposition product, or at least a more primary constituent than any characterized before. The large amount present contributes to the greater viscosity of such primary tars as compared with ordinary tars."

Commercially produced, low-temperature coal tars have lower degrees of "primariness," as Vahrman calls it, than true primary tar or even the vacuum distillate recovered by Juettner and Howard. The degree of primariness and the yield of any commercially produced tar is influenced by the extent to which the "bitumen" first distilled from the coal is subjected to secondary decomposition. As indicated by Damm (8), differences of kind and degree in the secondary decomposition are due to (a) the temperature to which the tar vapors become heated in their path from the heating chambers and (b) time of stay in the heating chambers. It follows, therefore, that tars having the highest degree of "primariness" are produced in coal-carbonizing devices in which the tar vapors are heated the least and for the shortest time. Conversely, coal tars with the least "primariness" are produced in high-temperature ovens or retorts in which the tar vapors are subjected to the most severe cracking and poly-

merizing conditions. As shown by Vahrman, the tars produced between these two extremes can be arranged in order of descending primariness depending on the types of equipment in which they are produced. A sequence of primariness similar to Vahrman's but somewhat modified and amplified is presented in Table IV.

TABLE IV. Sequence of "Primariness" in Descending Order for Coal Tars Produced in Various Types of Carbonizing Equipment.

Tar classification	Equipment type	Typical installations
Primary tar	High-vacuum still	Juettner and Howard
Low-temperature tar	Assay retorts	Fischer
	Thin-layer retorts	Borsig, Geissen, etc.
	Gas-circulation retorts	Lurgi, Parry, etc.
	Metal-chamber retorts	Krupp-Lurgi, Coalite, Brennstoff-Technik, etc.
Mid-temperature tar	Continuous, vertical, refractory ovens	H. Koppers, Didier-Werke, etc.
	Intermittent, slot-type, refractory ovens	H. Koppers, Carbolux, etc.
High-temperature tar	Continuous, vertical retorts	Woodall-Duckham, United Engineers, etc.
	Intermittent, vertical retorts	Woodall-Duckham, United Gas Improvement, etc.
	Horizontal retorts (full charges)	Gas Machinery Co., Russell Engineering Corp., etc.
	Slot-type coke ovens	Koppers Co., Inc., H. Koppers, Simon-Carv�s, Semet-Solvay, Wilputte, Otto, etc.
	Horizontal retorts (light charges)	Gas Machinery Co., Russell Engineering Corp., etc.

The manner in which tars produced in different types of carbonizing equipment are subjected to different amounts of cracking or pyrolysis and the variations in physical and chemical characteristics resulting therefrom have been discussed by Rhodes (33), Hansen (21), Damm (8), Vahrman (37), Forsdike (14), Pryde (32), Morgan and Soule (29), Coulson and Jones (7), and others. Fundamental aspects of the subject have also been extensively reviewed by Given (16) and by Bellington, Dryden, and Napier (5).

As previously mentioned, the coal from which a given coal tar is produced is another factor which may influence the characteristics of the tar, but the extent of the influence from this source depends largely on carbonizing conditions. As stated by Rhodes (33), "The nature of coal tar is influenced appreciably by the composition of the coal carbonized when carbonization is effected at low temperatures, but, under high temperature carbonizing conditions the influence of coal composition is largely or entirely overcome by the thermal decomposition of compounds which caused the tars produced at lower temperatures to have characteristic differences." On the other hand, "The yield of coal tar at all temperatures is influenced by the rank of the coal carbonized."

### Tar Distillation

When coal tar or coal-tar pitch is heated to elevated temperatures, some of the constituents polymerize or decompose and evolve permanent gases, even though the

original tar or pitch may have been produced under high-temperature conditions. The extent to which such alterations take place during distillation depends on the origin and nature of the tar distilled, the temperature at or to which the tar pitch is heated; the length of time during which it is exposed to cracking or polymerizing conditions; the amount of pressure or vacuum maintained during the distillation process; and the amount and kind of agitation employed (if any), that is, mechanical, air, steam, or inert gases. Thus product yields and characteristics from any given coal tar may vary appreciably with the type of distillation equipment employed and its method of operation. Fundamental considerations involved in the distillation of coal tar have been reviewed by Weiss (39,40), Moehle (28), Fischer (12), and others.

Many types of tar-distilling equipment have been used. They may be classified generally as batch and continuous. At first, batch stills were used exclusively. Small, vertical stills with concave bottoms were used for the most part in Great Britain and Europe, whereas horizontal, bottom-fired stills were generally preferred in the U.S. As the production of coal tar increased and the need for larger capacities, greater distillate yields, and improved economies became more important, attention was given to the development of continuous processes. Most of the early continuous installations consisted of vertical stills, arranged either singly or in multiple, for continuous operation. However, a few attempts were made to distill tar continuously by pumping it through a heated pipe coil and flashing it into a suitable chamber to separate vapors from pitch.

In the reviews by Weiss (39,40) the more important types of tar stills developed and used before 1926 were discussed. Since that time significant improvement has been made in tar-distilling practices, both in this country and abroad. Most of the improvement in the U.S. took place before 1940. The greatest improvements in British and European tar-distilling practices took place during and immediately after World War II.

#### BATCH STILLs

Extensive use is made of batch stills abroad. For the most part they are vertical, pot stills with concave bottoms. They vary in capacity from about 3,000 to 11,000 gallons per batch. In Germany they usually are operated under vacuum (about 600–650 mm. of mercury). Early stills of this type have been described by Warnes (38) and by Rispler (36). Illustrations and descriptions of modern, vertical 50-ton stills installed by some German tar distillers have been furnished by Deadman and Fuidge (9) and by Rhodes (34).

Vertical batch stills with cast-iron fractionating columns mounted directly on top were developed by Kahl (42) of Rütgerswerke A.G. in Germany and are still used extensively by that company to obtain distillate fractions sufficiently close-boiling for subsequent processing with little or no refractionation. They have been described in detail by Deadman and Fuidge (9) and illustrated by Rhodes (34).

The same authors also have described the internally and externally heated batch stills that are employed by some of the larger tar-distilling companies to obtain higher capacities and heating efficiencies. In such installations hot combustion gases flow first through two large tubes that are surrounded by the tar in the lower half of the still. The gases then flow along the lower outside surfaces of the still before passing to the stacks.

Horizontal stills of the internally and externally heated type mentioned above

have been used in the U.S. by at least one company since 1914. Another company has made extensive use of stills developed by Reilly (44) which are used for the production of pitch coke directly from coal tar in a single operation. The settings of such stills are so arranged as to have the entire exterior surface of the still surrounded by hot combustion gases to obtain more effective heating and to minimize the condensation of vapors. Other batch stills used in America are principally of the plain, bottom-fired, horizontal type. Little use is made of vertical pot stills in this country.

#### CONTINUOUS STILLS

**Continuous Single- and Multiple-Tank Stills.** Most of the early attempts to distill coal tar involved the use of one or more vertical or horizontal stills or tanks, connected and heated in such manner as to permit the simultaneous removal of one or more distillate fractions during the continuous distillation of the tar or pitch to the required softening point. In 1926 Weiss (39) described several continuous, tank-type installations. Of the various types mentioned by him, only those employing the principles developed by Abderhalden have maintained a position of commercial importance. Several installations of this type are operating in Europe and also in the U.S.

In 1927 the Koppers Co. equipped a horizontal internally and externally heated tar still for operation by the Abderhalden method. Crude or dehydrated tar was flowed continuously onto the surface of a reservoir of pitch having the desired softening point. The pitch was maintained at the temperature required to produce pitch of the same softening point from the incoming tar. Agitation of the pitch with superheated steam minimized the deposition of solids and coke formation on heating surfaces and also assisted in the removal of distillates. The capacities and distillate yields of existing batch stills to which this system was subsequently applied were substantially increased. Operations and products were further improved and diversified by the installation of columns and by coupling two batch stills of the same type for continuous operation in series. A particular advantage of this type of installation, aside from increased distillate yields, is flexibility. The individual units of such an installation may be used either for batch or for continuous distillation of any type of coal tar to pitch of any desired softening point up to approximately 325°F.

**Tube Stills (Pipe Stills).** A notable precursor of the modern tube still was a still installed before 1900 by Frederic Lennard (43) for the South Metropolitan Gas Co. near London. This still gave more than 50 years of continuous service. Further development of tube stills took place in the U.S. about 1913, but there was little interest in them abroad until much later.

**Single-Pass, Single-Flash Tube Stills.** In stills of this type the tar, usually after some preheating by heat exchange and separation of water by gravity or vaporization, is pumped through one heated pipe coil and released or "flashed" into a suitable chamber where separation of pitch and vapors takes place. The original Lennard still was of this type, and so were the Leinweber and Sadewasser stills, and the first tube stills installed by the Barrett Co. in the U.S. about 1913. In Leinweber's process low-boiling hydrocarbons are said to have been mixed with the crude tar before heating in the pipe coil to aid in the liberation of heavy oils from the pitch in the flash chamber. A distinctive feature of the Sadewasser installation was the use of a column to obtain a rough fractionation of the distillates. Fractionation was improved in later installations by Heinrich Koppers G.m.b.H. in Germany and elsewhere by the use of multiple

columns in series to separate the vapors leaving the flash chamber into 5 or more fractions. Later installations employed single columns with side streams rather than multiple columns. American and European installations of the latter type have been described by Wilson and Wells (41), Rhodes (34), Deadman and Fuidge (9), Bristow (6), Pound (31), and others.

At each of the installations mentioned above, liberation of the vapors from the pitch in the flash chamber took place at atmospheric pressure. In 1942 a still was designed by Gesellschaft für Teerverwertung in Germany in which dehydrated tar, heated in a single coil with a constriction at the outlet to prevent vaporization in the heater, was released into a vacuum flash chamber. In order to maintain a vacuum of about 80 mm. of mercury at this point, three packed columns of large diameter were used in series to recover carbolic oil, naphthalene oil, wash oil, and anthracene oil fractions. This installation has been described by Fischer (12), Rhodes (34), Deadman and Fuidge (9), and others.

Single-pass, single-flash stills of the types described above are employed principally abroad for the production of road tars and various grades of pitch used in the manufacture of carbon electrodes and for the briquetting of coal. They are seldom used for the production of pitches having softening points above 100°C. because of coking difficulties that accompany the use of the high temperatures required in such cases. In the U.S. stills of this type are used mainly for the topping of tars at steel plants where the soft or medium-hard pitches are used as produced or are fluxed with additional tar for the heating of open hearth furnaces.

**Double-Pass, Double-Flash Tube Stills.** The early development in America of outlets for pitches of high softening point created a need for tube stills having a greater range than the single-pass, single-flash stills discussed above. Two-stage tube stills were developed by the Barrett Co. to meet this need. As described by Weiss (40), preheated crude tar was flashed to remove water and light oil and then pumped through the first heating coil into a flash chamber. Soft pitch from this stage was then pumped through a second heating coil and flashed again to produce various grades of pitch with softening points between 180 and 300°F. Later this system of operation was largely superseded in America by a single-pass, double-flash operation.

After 1948 stills of the double-pass, double-flash type, designed by the H. Koppers organization, were installed abroad. Unlike the Barrett installation of similar type mentioned above, the primary purpose of these stills was not to produce pitches of high softening point but to make road tars and medium hard pitches for the briquetting of coal or for carbon electrode manufacture. Low tar temperatures, fuel economy, high distillate yields, close-boiling fractions, and minimum corrosion were stressed in the design of these installations. Partially dehydrated tar, heated by heat exchange with pitch and oil fractions, was pumped through a primary coil and flashed at atmospheric pressure in the base of a column which delivered light oil, carbolic oil, and naphthalene oil fractions. Soft pitch from the flash chamber at the base of the atmospheric column, after heat exchange in side stream reboilers and oil condensers, was pumped through a second coil and flashed in a vacuum chamber to remove wash oil and anthracene oil fractions. An additional feature claimed for this process was that, by maintaining the maximum temperature of the tar below 320°C., contamination of the anthracene oil by substances that interfere with anthracene crystallization was avoided.

During World War II a tar plant was installed at Espenhain, Germany, for the distillation of brown coal tar. The tar was distilled in two stages, atmospheric and

vacuum, with separate tube stills, flash chambers, and columns for each stage. The arrangement of the equipment has been described by Rhodes (35).

**Single-Pass, Double-Flash Tube Stills.** After its early experience with single-pass, single-flash and double-pass, double-flash tube stills, the Barrett Co. adopted a single-pass, double-flash system developed by MacCubbin and Zavertnik (46). In this process crude or partially dehydrated tar was pumped through only one heating coil, but the pitch leaving the primary, atmospheric flash chamber was drawn by vacuum into a secondary flash chamber where the vacuum caused additional vapors to be released and high softening point pitch to be produced without any further heating of the tar or pitch. According to Miller (27), the use of such equipment made it possible to produce pitch of 400°F. softening point without difficulty. Products of lower melting point could be recovered at temperatures below those in the usual tube stills operated at atmospheric pressure; distillate yields were increased and pitch yields decreased, and the pitch was of relatively low free-carbon content.

Plants of this type in use in the U.S. vary principally with respect to condensing and fractionating equipment. At some of them the vapors are fractionally condensed without columns to recover creosote and other wide-boiling distillates. Others are equipped with columns to obtain improved fractions for chemical recovery purposes.

**Recirculating Tube Stills.** In stills of this type, designed by Wilton's Patent Furnace Co., Ltd., crude tar, preheated in a light oil condenser, a waste heat coil, and a pitch-to-tar heat exchanger, enters a primary flash chamber where the water and light oil are released. The dehydrated tar then mixes with a large volume of hot pitch and releases additional vapors. The mixture of pitch and partially distilled tar is then pumped through a second heating coil and flashed into a chamber into which live steam is admitted to assist in the removal of more vapors. Excess pitch is withdrawn from this flash chamber, and the balance of the pitch is mixed with more dehydrated tar and recycled through the heating coil. The vapors from the three sources are fractionated by means of a column. A more complete description has been furnished by Wilson and Wells (41).

The large-diameter, cast-alloy heating tubes used in the Wilton stills are located in the convection sections of the furnace and are not exposed to any radiant heat. This arrangement and the use of pitch recirculation to increase the velocity and turbulence of the tar-pitch mixture passing through the coil minimize coke formation in the tubes so that infrequent cleaning is needed. This effect is also due in part to the fact that the use of such stills is limited principally to the production of pitches having softening points below 100°C.

**Combined Tube and Tank Stills.** The Abderhalden system of tar distillation which originally employed small, vertical, concave-bottom stills for heating the pitch on which the incoming tar was flashed with the aid of superheated steam was later improved by preheating the tar in a pipe coil before releasing it into the vaporizing still.

Operation of a typical unit installed in England in 1950 was as follows: Crude tar preheated by heat exchange in vapor coolers and by means of a cast-iron pipe coil, located in the final convection section of the furnace, was flashed in a dehydrating column to remove water and crude light oil. The latter was returned to the crude tar to serve as an entrainer for water and low-boiling oils. The mixture of dehydrated tar and crude light oil was then pumped through a pitch-to-tar heat exchanger and three banks of 2-in. I.D. cast-iron tubes. Vaporization in the heating tubes was

suppressed by means of a constriction near the outlet from which the heated tar flashed into a horizontal, stainless steel still in which pitch of the desired softening point was maintained at a constant level. The pitch in the still was agitated with superheated steam to decrease the partial pressure of the oils to be removed as distillates. Vapors from the still entered a column equipped for recovery of 7 fractions.

Although this type of installation was designed to use only convection heating of the pipe coils and horizontal still and to subject the tar only to a single-pass, single-flash type of operation, it was expected to produce pitches of any desired softening point up to 300°F. (149°C.).

### Coal-Tar Products

In the U.S. coal-tar products are made principally by commercial tar-distilling companies. However, as previously noted, several steel companies top or partially distill the coal tars from their coke-oven plants to obtain a topped tar (or soft pitch) which they use as fuel for open hearth furnaces. Some of them process the distillates recovered by such topping operations for the recovery of chemicals and creosote. In most cases, however, the distillates, usually called chemical oils, are sold to commercial tar-distilling companies which process them with distillates from coal tars purchased from other producers who do not carry on topping operations themselves.

The principal coal-tar products manufactured in the U.S. are coal-tar light oil, refined tar-acid oils, creosote, tar acids, tar bases, naphthalene, refined tars, road tars, industrial pitches, pitch coke and coatings. This list does not include benzene, toluene, xylenes, and solvent naphthas or their derivatives, which usually are designated as coal-tar chemicals but are derived in larger quantity from coal-gas light oil. The latter is a primary product of coal carbonization. It is recovered separately at coke plants by scrubbing the gas with wash oils from petroleum or coal tar (see *Benzene*).

Although the light oil contained in coal tar is higher-boiling than light oil recovered from coal gas, it contains small amounts of benzene, toluene, and xylene. In fact, benzene was first discovered in and recovered commercially from coal tar and became known as a coal-tar chemical. Later, when it was found that coal gas contained recoverable light oil with a much higher benzene content than coal tar, this became its principal source, but benzene continued to be called a coal-tar chemical. Actually, it is not possible to classify coal chemicals strictly as coal-tar chemicals, ammonia-liquor chemicals, light-oil chemicals, or coal-gas chemicals. The fractional condensation that takes place in the cooling and condensing equipment at coke plants produces primary products with overlapping compositions. This is illustrated by Table V, which lists the more important chemical constituents of each of the five primary products of coal carbonization, namely, coke and breeze, coal tar, ammonia liquor, light oil, and coal gas. The yields of various chemicals reported are not absolute for any given coke-oven tar or average for a certain group of tars. They were compiled from published data and from the results of various laboratory, pilot-plant, and chemical operations. They are intended only to represent the approximate commercial yields of various chemicals that might be expected from average typical products from present American coke-oven installations.

Also, it may be noted that the above list of commercial coal-tar products does not include the following materials, although they are listed as coal-tar chemicals in Table



TABLE V. Principal Chemicals Contained in the Primary Products from One Ton of Coal Carbonized in a Chemicals Recovery Oven.

Primary products and principal constituents	% contained in primary product	Lb. per ton of coal
Coke and breeze, 1,520 lb.		
Coke	92.7 (by wt.)	1410.00
Coal tar, 7.8 gal.		
Benzene	0.15 (by wt.)	0.12
Toluene	0.12	0.09
Xylenes	0.42	0.33
Pyridine	0.08	0.06
Intermediate tar bases	0.16	0.13
Quinoline	0.17	0.13
Coumarone and indene	0.25	0.20
Phenol	0.70	0.55
Cresols and cresylics	1.45	1.13
Naphthalene	8.00	6.24
1-Methylnaphthalene	0.50	0.39
2-Methylnaphthalene	0.05	0.39
Dimethylnaphthalenes	3.50	2.73
Acenaphthene	1.27	0.99
Diphenylene oxide	0.28	0.22
Fluorene	1.20	0.94
Phenanthrene	2.90	2.26
Anthracene	0.82	0.64
Carbazole	0.63	0.49
Fluoranthene	0.60	0.47
Pyrene	0.32	0.25
Chrysene	0.42	0.33
Totals	23.99 (by wt.)	19.08
Ammonia liquor		
Ammonium sulfate	—	20.0
Pyridine, crude	—	0.1
Phenol, crude	—	0.4
Total		20.5
Light oil, 2.8 gal.		
Carbon disulfide	0.5 (by vol.)	0.15
Cyclopentadiene	0.5	0.15
Benzene	57.0	11.68
Toluene	13.0	2.63
Xylenes	5.0	1.00
Coumarone and indene	5.0	1.26
Naphthalene	1.0	0.24
Totals	82.0 (by vol.)	17.11
Coal gas, 10,500 cu.ft.		
Hydrogen cyanide	0.2 (by vol.)	1.7
Hydrogen sulfide	0.7	6.7
Carbon dioxide	1.5	16.0
Carbon monoxide	5.8	43.2
Nitrogen	0.75	7.8
Hydrogen	57.2	30.4
Methane	29.2	132.0
Ethane	1.35	11.4
Illuminants		
Ethylene	2.50	19.6
Propane	0.11	1.4
Propylene	0.29	3.4
Butane	0.04	0.7
Butylenes	0.18	2.8
Acetylene	0.05	0.4
Light oil fraction	0.13	3.0
Totals	100.00 (by vol.)	280.5

V: methylnaphthalenes, dimethylnaphthalenes, acenaphthene, diphenylene oxide, fluorene, phenanthrene, anthracene, carbazole, fluoranthene, pyrene, chrysene. Although pilot-plant and semicommercial quantities of all of them have been made in the U.S., they are not now produced either individually or collectively in quantities comparable to those of the tar acids, tar bases, and naphthalene.

Anthracene (*q.v.*) was produced in sizable quantities during World War I. It was used for the production of the dye intermediate anthraquinone. However, shortly thereafter phthalic anhydride, made by the oxidation of naphthalene, replaced anthracene for this purpose in the U.S. In other countries the substitution of phthalic anhydride for anthracene in this connection has been more gradual, and anthracene is still an important coal-tar product.

Since about 1950 some of the other coal-tar chemicals mentioned above have been receiving an increasing amount of attention, particularly in Germany and Great Britain. As reported by Deadman and Fuidge (9) and also by Rhodes (34), several of them were made in commercial amounts in Germany during World War II. In Great Britain the production of such chemicals has been discussed recently by McNeil (25), Fowler-Williams (15), and others.

Brief discussions of the principal commercial coal-tar products manufactured in the U.S. follow.

**Coal-Tar Light Oil.** Coal-tar light oil is a low-boiling distillate that may be recovered from coal tar, although it is not always recovered as a separate fraction. It amounts to about 0.5–2% of average coke-oven tars and distills principally below 200°C. It contains small amounts of benzene, toluene, and xylenes, the remainder is referred to as "solvent naphtha." Solvent naphtha from coal-tar light oil is a source of raw materials for coumarone-indene resins (*q.v.*) that are used in the manufacture of floor tiles, linoleum, printing inks, waterproofing materials, rubber compositions, and varnishes. A larger source is the solvent naphtha recovered from coal-gas light oils. Coal-tar light oil is also used as such without fractionation for solvent purposes. Detailed information about the uses for light oil constituents has been furnished by Glowacki (17).

**Refined Tar-Acid Oils.** Refined tar-acid oils are solutions of tar acids (see p. 627) in low-boiling coal-tar oils. The tar-acid content may vary from about 10 to 55%, depending upon the use for which the tar-acid oil is intended. The oils are usually crystal-free at 0°C. (32°F.) and have an approximate boiling range of 180–250°C.

Refined tar-acid oils may be fractions recovered directly in the primary distillation of coal tar, but they are sometimes produced by dissolving tar acids in suitable coal-tar oils or by refractionation of tar-acid-containing oils.

Refined tar-acid oils are used principally in disinfectants, insecticides, flotation reagents, and heavy-duty cleaners. Disinfectants and insecticides of the milky-emulsion type are made by emulsifying refined tar-acid oil with water, using a suitable soap as the emulsifying agent. They are used for general disinfection purposes and as animal dips. When used for recovery of minerals by froth flotation processes, refined tar-acid oils may be used as produced or after modification with other chemicals. Heavy-duty cleaners made by the emulsification of tar-acid oils are used principally for the degreasing of engine and machine parts.

**Creosote.** Coal-tar creosote was first used for the preservation of wood by Bethell in England in 1838. Since that time it has been a principal product of coal-tar distillation in each of the major tar-producing countries. U.S. production of creosote

in 1953 amounted to 138.7 million gallons. This was approximately 24.4% of all coal tar distilled and about 17.4% of all coal tar produced in that year.

Creosote is defined by the American Wood Preservers Association as follows: "As used in wood preserving, creosote is a distillate of coal tar produced by high temperature carbonization of bituminous coal. It consists principally of liquid and solid hydrocarbons and contains appreciable quantities of tar acids and tar bases; it is heavier than water and has a continuous boiling range of at least 125°C. beginning at about 200°C."

About 18% of the creosote produced in the U.S. is mixed with coal tar before shipment to consumers. Such mixtures, usually containing 20–40% of coal tar, are called creosote-coal-tar solutions. Most users of creosote and creosote-coal-tar solutions in the U.S. require that they shall comply with standard specifications of the American Wood Preservers' Association (4) or the American Railway Engineering Association. The production of creosote at tar-distilling plants consists in the selection or combining of coal-tar distillates to meet such specifications.

Creosote and creosote-coal-tar solutions are used for the preservative treatment of railway cross ties, telephone and telegraph poles, cross arms, fence posts, marine and foundation piling, wood blocks and timbers for buildings, tanks, bridges, and other structures to protect them against attack by fungi, marine borers, or insects. Standard methods for the preservative treatment of wood for the various purposes mentioned above are recommended by the American Wood Preservers' Association (4).

**Tar Acids.** Tar acids, often referred to collectively as "phenols," are constituents of coal-tar distillates that are soluble in dilute caustic soda, giving sodium "cresylate." The bulk of the tar acids in coke-oven tars and other high-temperature coal tars may be concentrated by fractionation in that portion of the total distillate distilling below approximately 235°C., which is usually termed *tar-acid oil* or *chemical oil*. The chemical oil fraction amounts to about 10–20% of average coke-oven tars. Washing of the chemical oil with a dilute solution of caustic soda removes most of the tar acids, together with traces of oils and tar bases. These impurities are removed from the sodium cresylate by steaming and evaporation. The purified cresylate is then blown with lime kiln or combustion gases containing carbon dioxide to liberate crude tar acids. After reblowing with gas containing carbon dioxide and treatment, if necessary, with mineral acid to complete their liberation and to lower their water content, the crude tar acids are dehydrated and fractionated to yield various grades of phenol, *o*-cresol, *m-p* cresol mixtures, and higher-boiling tar-acid fractions containing mixtures of the six isomeric xylenols. See *Cresols*; *Phenol and phenols*.

The uses for tar acids in the U.S. are numerous. They include phenolic resins or plastics of the cast-molding, laminated, water-soluble, and oil-soluble types, soluble and emulsion-type disinfectants, mineral flotation reagents, synthetic tanning materials, paint and varnish removers, plasticizers, drugs, perfumes, explosives, and a great variety of synthetic organic chemicals.

**Tar Bases.** Tar bases, also described as nitrogen bases or pyridine bases, are cyclic, nitrogen-containing compounds that are present in coal carbonization ammonia liquors, coal-tar light oil, and coal gas. They are soluble in dilute mineral acids. They include pyridine, picolines, lutidines, collidines, aniline, toluidines, xyloidines, quinoline, isoquinoline, quinaldines, and higher-boiling bases. In the U.S., coke-plant ammonia liquor is the principal source of the lower-boiling tar bases, that is, pyridine, picolines, and lutidines; whereas coal tar is the principal source of the higher-

boiling tar bases. The latter are obtained from the chemical oil fraction boiling below 235°C. usually after the tar acids have been extracted as described above.

Extraction of the tar bases is accomplished by washing the chemical oil with dilute sulfuric acid. Caustic soda is added to the tar-base-sulfate solution to liberate crude tar bases. The latter are then distilled to obtain close-boiling fractions. In recent years quinoline (*q.v.*) has been the principal product obtainable from this source. It has been used principally in the manufacture of nicotinic acid and 8-hydroxy-quinoline. High-boiling tar bases are used also in the manufacture of pickling inhibitors and various synthetic organic chemicals.

**Naphthalene** (*q.v.*). From the standpoints of commercial production and usage, the most important coal-tar chemical is naphthalene. It also is the largest single constituent of high-temperature coal tars, averaging as shown in Table III about 9.6% in American coke-oven tars in 1952. It is contained in the same chemical oil fractions boiling below approximately 235°C. that are processed for tar acids and tar bases as described above. It is recovered therefrom as crude naphthalene ("naphthalene salts") at tar-distillation plants and tar-topping plants by various methods involving fractionation or crystallizing and centrifuging procedures.

Various grades of crude naphthalene are produced ranging in freezing point from about 74 to 79°C. For purposes requiring a higher degree of purity the crude naphthalene is washed with concentrated sulfuric acid, neutralized with caustic soda, and fractionated to obtain refined naphthalene having a minimum freezing point of about 79.6°C. The principal use for crude naphthalene is the production of phthalic anhydride by catalytic oxidation (see *Phthalic acids*). Refined naphthalene is used principally for the production of dye intermediates, chlorinated naphthalene, and numerous synthetic organic chemicals. More complete information about naphthalene and other chemicals obtainable from coal tar has been furnished by Rhodes (33).

The chemical oil, from which the tar acids, tar bases, or naphthalene may have been recovered, may be used with higher-boiling coal-tar oils in creosote and creosote-coal-tar solutions.

**Refined Tars.** Refined tars are dehydrated, partially distilled, or fluxed coal tars that are used in the manufacture of various coal-tar paints and coatings and as saturants for felts and fabrics used with coal-tar pitch for roofing and waterproofing purposes. Also, they are used for the preservative treatment of fish nets and ropes and for rubber-softening, reclaiming, and compounding purposes. Usually refined tars are made to comply with customers' specifications or use requirements.

**Road Tars.** Coal-tar road materials have been used in the U.S. for the construction and maintenance of highways since about 1870. Special methods have been developed for the use of road tars, including the stabilization of soil bases, prime coating of subgrades, hot and cold surface treatments, drag leveling courses, mulch treatments, road mixes, penetration construction, tar-concrete construction, joint and crack filling, and hot and cold patching. This large variety of maintenance and construction methods requires the production and use of road tars having a wide range of consistencies. Within this range, twelve grades of road tar designated RT-1 to RT-12 and two grades designated RTCB-5 and RTCB-6 are recommended by the American Society for Testing Materials (3) and the American Association of State Highway Officials (1). The specifications of these two societies have been adopted by most of the major users of road tars in the U.S. See also *Asphalt (uses)*.

The RT-1 to RT-12 grades of road tar are generally made by blending or straight distillation procedures. Blending agents may consist of water-gas or oil-gas tars or

distillates therefrom. The RTCB-5 and RTCB-6 grades contain volatile solvents to accelerate their rate of set-up when used for patching purposes.

Following are some of the characteristics which make road tars especially suitable for road construction and maintenance purposes: deep penetration without segregation into soils and small openings in or between aggregate particles; superior adhesion to aggregate surfaces; resistance to water; insolubility in lubricating oils, gasoline, diesel oils, and jet fuels; and skid resistance.

**Roofing and Waterproofing Pitches.** Because of its extreme resistance to penetration and destruction by water and because of self-healing characteristics resulting from cold flow, coal-tar pitch is a superior waterproofing material for flat roofs on buildings and for reservoirs, bridge decks, tunnels, foundations, dams, retaining walls, and structures of other types (see *Bituminous roofing materials*). The pitch is usually applied to such structures between alternate plies of coal-tar saturated felt or fabric. In the case of roof decks, bridge decks, and other horizontal surfaces, the three-, four-, or five-ply membrane formed in this manner is covered with slag or gravel. Roofing and waterproofing pitches and tar-saturated felts and fabrics usually are made to comply with the requirements of standard specifications promulgated by the American Society for Testing Materials and the Federal Specifications Board.

**Fiber Pipe and Conduit Pitch.** Large quantities of coal-tar pitch are used for the impregnation under vacuum of fiber pipes or tubes which are used as electrical conduits and for drainage purposes. Coal-tar pitch is superior for such purposes because of its resistance to water, fungi, tree roots, and acid or alkaline soil conditions. It is made from selected coal tars to meet customers' specification requirements.

**Briquet Pitch.** The largest single use for coal-tar pitch abroad since the early days of the coal-tar industry has been the briquetting of coal. Coal fines are mixed with about 5-8% of coal-tar pitch, heated sufficiently to melt the pitch, and pressed to form blocks or fuel briquets of various sizes and shapes. Coal-tar pitch was used extensively for this purpose in the U.S. before 1920, but other markets have absorbed most of the pitch in recent years.

**Carbon Electrode Pitches.** Coal-tar pitch is a preferred binder for use in the manufacture of amorphous and graphitized electrodes, blocks, cylinders, powders, and other carbon products (see *Carbon (baked and graphitized)*). The pitch is mixed with petroleum coke, pitch coke (see p. 630) metallurgical coke, lampblack, carbon black, or combinations of such materials; the mixtures are pressed, extruded, or molded to obtain the desired shapes and are then heated slowly to the required temperatures. Coal-tar residuals used for this purpose range in consistency from low-viscosity tars to high-softening-point pitches. They are usually produced to meet customers' specifications.

Coal-tar pitch is especially suitable for this application because it contains very little ash or sulfur and has a high content of resinous materials which yield coke when carbonized at relatively low temperatures. The formation of this coke between the grains of solid carbonaceous materials comprising the bulk of the structure cements the latter together into a dense and highly conductive product.

**Target Pitch.** The brittleness of hard coal-tar pitch makes it especially suitable for the production of clay pigeons used as targets in such sports as trap-shooting and skeet-shooting. The targets are made by mixing high-softening-point coal-tar pitch with a suitable filler such as limestone dust, heating the mixture, and forming it into saucer-shaped disks. Owing to the brittleness of the pitch binder, the target disintegrates when struck by one or more pellets from a shot gun shell.

**Core Binders.** Core compounds containing high-softening-point pitches are used extensively in the preparation of foundry molds and cores. Sand, clay, and core compounds are intimately mixed, moistened with water, and rammed into or around a pattern having the shape and dimensions of the desired casting or cavity. The pattern is then removed from the mold or core, and the latter is baked to remove moisture and to melt and carbonize the core compound sufficiently to cement the sand and clay particles firmly together.

After the molds and cores have been used in the foundry, they are disintegrated and conditioned for re-use by the addition of more core compound. The suitability of coal-tar pitch for this purpose is due to its inherent binding capacity, which imparts strength to the molds and cores prior to and during the casting of the metal.

**Pitch Coke.** Pitch coke is used in the manufacture of prebaked and Soderberg-type electrodes. See *Carbon (baked and graphitized)*. It also is used in foundries, in open hearth furnaces, and in the manufacture of silicon carbide and other carbon compounds. It is especially suitable for such purposes because of its low ash and sulfur contents.

The principal methods that have been used in the U.S. for the manufacture of pitch coke are:

**Reilly Method.** Coal tar is distilled to coke in stills that are heated over their entire exterior surfaces to prevent cooling and refluxing of the higher-boiling distillates. The pitch coke remaining in the still at the end of the distillation period is quenched with water and removed through a manhole on one end of the still. The coke contains about 6 or 7% of volatile material.

**Barrell or Hall Process.** Pitch having a high softening point is carbonized in beehive ovens. Coke made by this process is extremely dense and hard and is almost completely devolatilized.

**Koppers Method.** Molten, high-softening-point pitch is pumped from the still in which it is produced or from an intermediate, heated feed tank through a loop passing over the tops of slot-type coke ovens. Molten pitch is charged into an oven from the overhead loop during a period of approximately 3 hours. The charge of pitch is then carbonized, and the coke is pushed from the oven and quenched in the usual manner. The finished product contains less than 1% volatile matter.

**Enamels and Coatings.** Hot-application enamels made from coal-tar pitch and suitable fillers are used for the protection of iron and steel surfaces against corrosion. Internal and external surfaces of steel ships, dry docks, lock gates, penstocks, water lines, oil lines, gas lines, underground tanks, sheet piling, and H piling are typical structures of the types that are protected with coal-tar enamels. Their extreme resistance to penetration by water and to the destructive effects of soil conditions has been largely responsible for their outstanding success when used for such purposes.

Coal-tar coatings, suitable for cold application by brush or spray methods, are used for the protection of steel structures above ground and sometimes underground when corrosive conditions are not so severe as to require the use of hot-applied enamels.

**Coal-Tar Fuels.** Coal tars and tar residuals are used for fuel purposes both in this country and abroad. Foreign practice usually consists in atomizing the molten pitch alone or in combination with creosote into the combustion chamber of the still, boiler, or other type of unit to be heated. The largest users of coal-tar fuels in the U.S. are steel plants. A method for pulverizing and burning high-softening-point pitch developed by E. W. Clarke (45) has been used extensively in the U.S. Coal-tar fuels

are especially desirable for certain purposes where low ash and sulfur contents or highly luminous flames are desirable.

Industrial and motor fuels have been produced commercially abroad by the hydrogenation of coal tars and coal-tar oils, but for economic reasons similar developments have not taken place in this country.

### Water-Gas and Oil-Gas Tars and Pitches

Water-gas and oil-gas tars are recovered from manufactured gas when the latter is produced by the cracking or gasification of petroleum distillates or residuals in carbureted-water-gas and oil-gas generators (see *Manufactured gas*).

Water-gas manufacture has been extensively reviewed by Morgan (28a), and oil-gas manufacture by Hull and Kohlhoff (24), Hall (20), and others. Also, variations in the yields and characteristics of water-gas and oil-gas tars, distillates, and pitches have been discussed by Martin (26), the American Gas Association (2), and others.

In the earlier years of water-gas manufacture, oils used as carburants were of the petroleum-naphtha or gas-oil types. The water-gas tars recovered from the gas made from such carburants were low in specific gravity, viscosity, benzol-insoluble material, and pitch content. They were used principally as fluxes in the production of cold-application road materials from high-viscosity coal tars. Light water-gas tars and various distillates and pitches derived therefrom also were used in the manufacture of certain types of bituminous paints and coatings, shingle stains, conduit saturants, and, in combination with zinc chloride, for the preservative treatment of wood.

In recent years the use of light petroleum distillates for water-gas manufacture has been uneconomical, and processes have been adapted to the use of heavy petroleum residuals. Water-gas tars produced from such carburants have much higher specific gravities, viscosities, benzol-insoluble, and pitch contents. Also, their yields per gallon of carbureting oil are much greater than the yields of light water-gas tars from naphthas and gas oils. Because of their high viscosities the heavy water-gas tars are not suitable as fluxes for cold-application road tars. However, they are used alone and in combination with coal tars for the production of various grades of tar road materials. This also is the principal outlet for oil-gas tars.

### Bibliography

- (1) American Association of State Highway Officials, Standard Specifications for Tar for Use in Road Construction, Specification M-52.
- (2) American Gas Association, "Characterization of Water-Gas Tars," Gas Production Research Committee, Research Bull. 2.
- (3) American Society for Testing Materials, Standard Specification for Tar, D 490-47.
- (4) American Wood Preservers' Association, *Manual of Recommended Practice*, 1953.
- (5) Bellington, A. H., Dryden, I. C. C., and Napier, D. H., *Bull. Brit. Coal Utilization Research Assoc.*, Review 115, Part I, 12, No. 6 (June 1952).
- (6) Bristow, W. A., *J. Inst. Fuel*, 20, No. 113, 109 (1947).
- (7) Coulson, E. A., and Jones, J. I., *Coke Smokeless-Fuel Age*, 8, 108, 120 (1946).
- (8) Damm, P., *Erdöl u. Kohle*, 4, 765 (Dec. 1951).
- (9) Deadman, A. L., and Fuidge, G. H., *B.I.O.S.*, 25 (1950).
- (10) Denig, F., "Industrial Coal Carbonization," in *Chemistry of Coal Utilization*, H. H. Lowry, ed., Wiley, N.Y., 1945.
- (11) Fieldner, A. C., and Davis, J. D., *U.S. Bur. Mines Monograph*, 5 (1934).
- (12) Fischer, W., *Z. Ver. deut. Ing. Beiheft Verfahrenstechnik*, No. 1, 13 (1944) (Tech. Oil Mission, Microfilm Reel 150).

- (13) Fisher, C. H., *U.S. Bur. Mines Bull.*, **412** (1938).
- (14) Forsdike, R., *Gas World*, **136**, 350 (1952).
- (15) Fowler-Williams, A., *Intern. Chem. Eng. & Process Inds.*, **132**, 159 (1951).
- (16) Given, P. H., *Bull. Brit. Coal Utilisation Research Assoc.*, Review 115, Part II, **12**, No. 6 (June 1952).
- (17) Glowacki, W. L., "Light Oil from Coke-Oven Gas," in *Chemistry of Coal Utilization*, H. H. Lowry, ed., Wiley, N.Y., 1945.
- (18) Gluud, W., and Jacobson, D. L., *International Handbook of the By-Product Coke Industry* Chemical Catalog Co., N.Y., 1932.
- (19) (Great Britain) Colonial Geological Surveys, Mineral Resources Division, *Statistical Summary of the Mineral Industry, Production Imports and Exports 1945-1951*; H.M. Stationery Office, London, 1953.
- (20) Hall, E. L., *Chem. Met. Eng.*, **48**, 100 (1941).
- (21) Hansen, C. J., *Brennstoff Chem.*, **31**, No. 19/20, 308. (1950)
- (22) Juettner, B., and Howard, H. C., *Ind. Eng. Chem.*, **26**, 1115 (1934).
- (23) Keeling, W. O., and Jung, F. W., "Carbonization," in *Encyclopedia of Chemical Technology* Vol. 3, R. E. Kirk and D. F. Othmer, eds., The Interscience Encyclopedia, Inc., N.Y., 1949.
- (24) Hull, W. O., and Kohlhoff, W. G., *Ind. Eng. Chem.*, **44**, No. 5, 936 (1952).
- (25) McNeil, D., *Gas World* (Sept. 1, 1951).
- (26) Martin, S. W., *Proc. Am. Wood-Preservers' Assoc.*, **49**, 100 (1949).
- (27) Miller, S. P., *J. Franklin Inst.*, **215**, No. 4, 373 (April 1933).
- (28) Moehrl, E., *Gluckauf*, **14**, 302 (April 3, 1937).
- (28a) Morgan, J. J., *American Gas Practice*, 2nd ed., J. J. Morgan, Maplewood, N.J., 1945.
- (29) Morgan, J. J., and Soule, R. P., *Chem. Met. Eng.*, **26**, 1025 (1922).
- (30) Porter, H. C., *Coal Carbonization*, Chemical Catalog Co., N.Y., 1924.
- (31) Pound, G. S., *J. Inst. Fuel*, **24**, 61 (1951).
- (32) Pryde, D. R., *Gas World*, **101**, 108 (1934).
- (33) Rhodes, E. O., "The Chemical Nature of Coal Tar," in *Chemistry of Coal Utilization*, H. H. Lowry, ed., Wiley, N.Y., 1945.
- (34) Rhodes, E. O., *U.S. Bur. Mines Inform. Circ.*, **7409** (Sept. 1947).
- (35) Rhodes, E. O., *U.S. Bur. Mines Inform. Circ.*, **7490** (Feb. 1949).
- (36) Rispler, A., *Chem. Ztg.*, **34**, 261 (1910).
- (37) Vahrman, M., *J. Appl. Chem. (London)*, **2**, 532 (Sept. 1952).
- (38) Warnes, A. R., *Coal Tar Distillation*, 3rd ed., Ernest Benn, Ltd., London, 1923.
- (39) Weiss, J. M., "Tar Refining and Tar Products," in Report of Chemistry Committee, American Gas Association, 1926.
- (40) Weiss, J. M., *Chemistry & Industry*, **10**, 219, 246 (1932).
- (41) Wilson, P. J., and Wells, J. H., *Coal, Coke and Coal Chemicals*, McGraw-Hill, N.Y., 1950.
- (42) Brit. Pats. 208,691 (Sept. 4, 1923); 221,773 (March 11, 1924), L. Kahl.
- (43) Brit. Pat. 844 (Dec. 19, 1891), F. Lennard.
- (44) U.S. Pat. 1,230,782 (June 19, 1917), P. C. Reilly.
- (45) U.S. Pat. 1,660,831 (Feb. 28, 1928), E. W. Clarke.
- (46) U.S. Pat. 1,759,816 (May 20, 1930), A. A. MacCubbin and J. Zaverbnik, Jr.

E. O. RHODES

**TARAXEROL**,  $C_{30}H_{50}O$ ; **TARAXESTROL**,  $C_{30}H_{50}O$ . See *Terpenes (tri-)*.

**TARIRIC ACID**,  $CH_3(CH_2)_{10}C:C(CH_2)_4COOH$ . See *Fatty acids*, Vol. 6, p. 177.

**TAR OILS**. See *Tar and pitch*.

**TARRAGON OIL**. See "Estragon" under *Oils, essential*, Vol. 9, p. 581.



## TAR SANDS

Tar sands (also known as oil sands and bituminous sands) are sands that are impregnated with a heavy petroleum. The largest and most important deposits are the Athabasca sands, found in northern Alberta, Canada. The name tar sand was given by early observers, because of the asphaltic appearance of the sand deposits. Later, geologists referred to them as bituminous sands, and since the interest in their possible use as a source of oil, they have also been termed oil sands. Actually, since they contain a heavy petroleum, neither tar sands nor oil sands is the best term, but tar sand is well established by long usage and will probably persist. The tar sands have been extensively investigated as a source of petroleum products. See also *Fuels, synthetic liquid*; *Petroleum (refinery processes)*; *Shale oil*.

Oil sand or similar deposits are found in most areas of the world where petroleum is found. The oil in these surface and near-surface deposits is often the result of weathering of a lighter oil that has seeped into the sand beds. The sands were excavated or drained from hand-dug wells in France, Poland, Rumania, Russia, the Middle East, and the Far East for years until modern drilling methods were used to tap the main oil reservoir (17). It is interesting to note that when the oil wells in some of these fields ceased to produce, there was a return to underground workings on an extensive scale (18). Surface and near-surface deposits of oil-impregnated sands also occur in many places in the United States (9). Those in Kentucky became well known because of their exploitation for road building. Large deposits of sands also occur in California and Utah (21). (See p. 643.) However, all of these oil-sand occurrences are small in comparison with the Athabasca oil-sand deposit.

### Athabasca Tar Sands

The Athabasca oil sands lie in the north of the province of Alberta and outcrop along the Athabasca River and its tributaries for sixty miles north of McMurray (see Fig. 1). The area indicated by outcrops as being underlain by the formation is at least 2,000 square miles in extent. The Northern Alberta Railway has a line running east of north from Edmonton for about 300 miles to Waterways on the Clearwater River a few miles from McMurray. The Athabasca River is navigable and is the highway for freighting into the far north. McMurray is an airport on the airlines to the uranium and gold-mining camps on Lake Athabasca, Great Slave Lake, and Great Bear Lake.

Canadian government geologists were the first to give scientific attention to the Athabasca oil sands. R. G. McConnell, in 1890-91, examined them during his reconnaissance of the Athabasca district (14). He considered that the oil as seen at outcrops was the residuum from evaporation of petroleum that entered the sand formation from the Devonian shales and limestones immediately below. He recommended drilling at a site far removed from outcrops and where the sands were well covered by consolidated strata in order to tap the oil in its original fluid state. This drilling was done during 1897-98 at Pelican Rapids on the Athabasca River about 80 miles southwest of McMurray (22,23). The oil sands were reached at a depth of 740 ft. through shales and sandstones. The oil in the sand was the same heavy oil found at outcrops. Since then, various exploratory holes have been drilled in the oil sands at widely scattered points far from outcrops and this heavy oil has been found.

Further study of the oil sands was begun in 1913 by S. C. Ellis, whose work included mapping, and the demonstration of the use of tar sands as road material (10). Work has been continued on different aspects of oil sand by the Research Council of Alberta, formed in 1919 (7). Commercial developments included that of Abasands Oils, Ltd., which operated a quarry and hot-water-separation

plant intermittently from 1935 until 1943 (2). During 1941 a possibility of an oil shortage due to Japanese threats to shipping led to further exploration for oil-sand mining areas (12,24). During part of 1949, the Government of Alberta operated a 500-ton-per-day plant for the separation of oil by

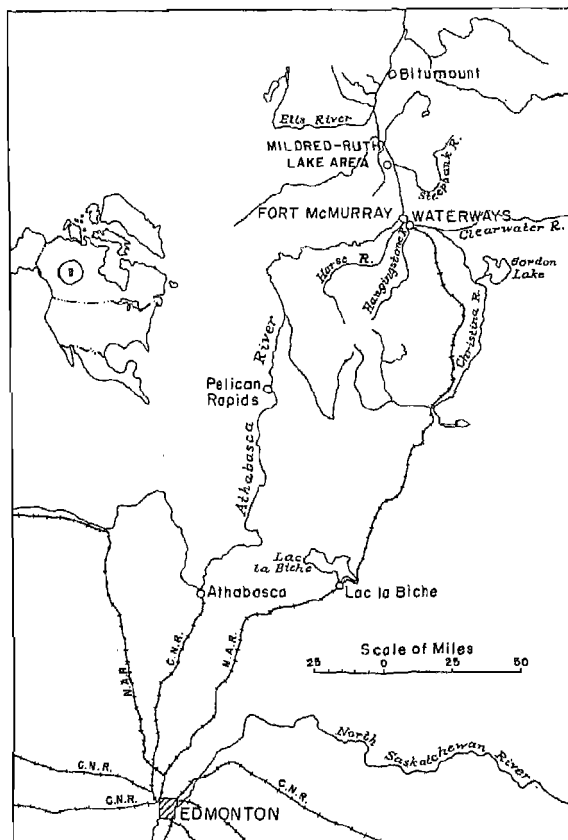


Fig. 1. Location of the Athabasca oil sands.

hot-water extraction. It operated successfully and showed that the hot-water method was satisfactory (1). In 1950 the "Blair report," the result of a survey headed by S. M. Blair, was published (3). This survey concluded that profitable operation of oil-sand developments was a present-day possibility. During 1952, eleven permit areas of about 50,000 acres each were reserved by oil companies for exploration, and by the end of 1953 about 150 holes had been drilled and logged.

#### THE OIL SAND FORMATION

The Athabasca oil-sands deposit, known geologically as the McMurray formation, is of Lower Cretaceous age. It lies unconformably on Devonian limestone and shale of Upper Devonian age. It is overlain by marine shales, called the Clearwater formation. No clear evidence that the McMurray formation is marine has been found and it is generally assumed to be of fresh or brackish water origin. The stratigraphic column is:

##### Lower Cretaceous

Grand Rapids formation: sandstone and shale.

Clearwater formation: gray and dark marine shales.

McMurray formation: bituminous and fine-grained sands, in part cross-bedded and lenticular interstratified with clay and shales. Thin lignite seams and plant material.

Erosional disconformity.

## Upper Devonian

Waterways formation: shaly and massive fossiliferous limestone, in places overlain by residual limy clay of variable thickness.

The Clearwater shales have been eroded away over much of the outcrop area north of McMurray. Their occurrence east of the Athabasca River is fragmentary. West of the river they are generally absent for several miles but are probably present from there westward. The Grand Rapids formation of shales and sandstones outcrops along the Athabasca River south of the outcrop area, and is exposed to the west of this outcrop area along Ells River. The surface layer over the outcrop area consists of recent sandy material from a few feet to over a hundred feet thick (25).

**McMurray Sediments.** The sediments of the McMurray formation consisting of sand, silt, and clay were deposited on the detritus covering the Devonian floor. They are very irregular in nature varying from those in which silt and clay dominate the aggregate and form what can be termed shale, to sand in which silt and clay, although present, are not obvious. There are no persistent beds of either shale or sand. Sections half a mile apart cannot be correlated closely and often are totally different. Sections above the old river trench consist mainly of shale. On the other hand, the highest Devonian ridge so far found is covered mainly with sand. Elsewhere, sections consist of a variable accumulation of shale, sand, and interbedded shale and sand. The sediments are unconsolidated. Some minor induration is present in most sections. The top of the McMurray sediment reflects only slightly the topography of the Devonian floor. Frequently, it is thicker over low areas in the Devonian than over high. In general, it varies in thickness from 125 to 200 ft., although some sections over the old trench are 400 ft. thick.

A highly fossilized lens of oil sand and sandstone appears toward the top of the McMurray formation on a high cutbank on the Hangingstone River near McMurray. Small gastropods and pelecypods are present in profusion. These fossils are considered to indicate a fresh-water environment although the presence of some genera suggest proximity to the sea (19). Hume reported that marine shale containing foraminifera and small pelecypods was found interstratified with oil sand in a drill hole in the Mildred-Ruth Lakes area (12). Black, carbonized wood, from small fragments to tree trunks, occurs in the sand beds. The grain and even the cell structure is preserved. Fragments of the stem and leaf structure of reedy plants are contained in the shale beds. Some of these are blackened by their content of organic material.

Sand particles consist of quartz predominantly, but include a few per cent of particles of mica, rutile, zircon, tourmaline, and pyrite. The silt has not been studied closely but it appears to be similar to the sand in composition. Some clay material is generally present. The quartz grains are sub-angular in shape and a considerable proportion of them have frosted surfaces. Most of the sand grains are smaller than 80-mesh size.

**McMurray Oil.** The oil in the McMurray oil sand varies in specific gravity (25°/25°C.) between 1.002–1.027. Its ultimate analysis is quite constant both vertically and laterally throughout the formation. An analysis of oil from the quarry at Bitumount shows:

Carbon.....	83.3%
Hydrogen.....	10.4%
Sulfur.....	4.7%
Nitrogen.....	0.4%
Oxygen(diff.).....	1.2%
C/H ratio.....	8.0
Caloric value, B.t.u./lb.....	17,910

Sulfur varies between 4.0–5.5%; nitrogen between 0.4–0.6%.

The analysis of the oil in terms of asphaltenes, resins, and oily constituents (solvents: ethyl ether, *n*-pentane, and benzene) varies with the specific gravity. The ranges of variation are (15):

Asphaltenes.....	17–21%
Resins.....	25–29%
Oily constituents.....	48–59%

The oil is very viscous. In this connection it is to be noted that the formation temperature of the McMurray deposit is low, ranging from 36–40°F. At 40°F., viscosity varies with specific gravity between 10,000 and 5,000,000 poises; at 200°F., between 2 and 10 poises (29).

**Oil Sand.** The oil entered the McMurray sediments, impregnating them more or less completely. The sandy beds are well impregnated and are high-grade oil sand. There is definite correlation between the oil content and material in the oil-sand aggregate that passes the 200-mesh sieve. In general, a content up to 20% through 200-mesh material has not affected impregnation. But as the content of minus 200-mesh material increases, the oil content decreases to low values. "Material passing the 200-mesh sieve" is too indefinite a basis on which to seek close relationships. The porosity of good-grade oil sand is high, varying between 35 and 45%. Total liquid saturation varies from 90 to 100%. The average oil and water contents for oil-sand samples with oil contents of 10% by weight or more are about 14% oil and 3% water. The shaly phases of oil sand have high water contents and correspondingly low oil contents.

Water is present in the oil sand as a disperse phase in the oil and also as bulk water. Small oil seepages are fairly common around outcrops. A sample of seepage oil that appears to be dry will show a water content of about 20% on analysis. The wet oil does not adhere to the sand surfaces, and there seems to be a film of water separating them. When a hole is augered into an oil-sand face, the cuttings appear gray. Under magnification, they are seen to consist of a mixture of clean, white quartz grains and black oily masses.

Good grade oil sand at or near the formation temperature is a firm, stable material. Although unconsolidated, the content of viscous oil at low temperature holds it together tenaciously. When warmed by summer weather as at a quarry face, a small power shovel can dig in the oil sand readily, but it becomes ineffective beyond the warmed surface layer.

A good grade of oil sand weighs about 125 lb./cu.ft. Its coefficient of thermal conductivity is of the order of 0.0035 in c.g.s. units. The specific heat of the mineral aggregate is 0.18 cal./gram and that of the oil is 0.35 cal./gram (6).

#### ORIGIN

Data on which to base conclusions about the origin of the McMurray sediments and of the oil present in them are still meager. Most geologists who have studied the oil sands consider that the deposit is an alluvial fan or deltaic formation with the sediments derived from the Athabasca sandstones to the east and other pre-Cambrian rocks (25).

Geologists are divided sharply over the question of the origin of the oil. One group contends that it entered the McMurray sands from reefs in the Devonian limestone. The sands lie unconformably on the truncated Devonian beds which contain such oil-bearing reefs as those of the Leduc and Redwater oilfields. Other geologists argue for a Lower Cretaceous origin for the oil. The issue was debated at the Oil Sands Conference (25).

Chemical evidence that seems to bear on the question of the origin has been contributed by recent work. The content of vanadium and nickel in the oil-sand oil is comparatively high. It is nearly constant throughout the McMurray formation, both

vertically and laterally, at about 360 p.p.m.  $V_2O_5$  and 106 p.p.m. NiO. The interesting observation in regard to origin is that the ratio of vanadium to nickel is approximately the same for almost all Alberta crude oils produced from basal Cretaceous reservoirs, and that this ratio is entirely different for oils from Devonian reservoirs. The data indicate clearly that the oil-sand oil is a normal member of the family of crude oils found in the basal Cretaceous horizons, and is not unique among crude oils. In addition, a study of the manner of occurrence of the vanadium and nickel in the oils has yielded further evidence on the nature of the oil. The metals occur in porphyrin structures, derived in all probability from chlorophyll. The presence of the metal-containing porphyrins in the heavy black oils of the basal Cretaceous horizons and the apparent absence of similar structures in the lighter oil from the basal Cretaceous horizons are taken to indicate that the heavy black oils, including the oil-sand oil, must be regarded as precursors, rather than residue products of the lighter oils (20). A study on the preparation of asphalts by vacuum distillation of the oil from Athabasca tar sands (11a) showed that the initial cracking temperature of the oil was very low in comparison with all the other crude oils studied in this manner. This is further confirmation that the Athabasca oil must be regarded as a precursor rather than a residue of some other oil.

#### RECOVERY

**Hot-Water Washing.** The Athabasca oil sands are very amenable to the separation of oil from sand by washing with water, especially hot water. Soluble salts in significant quantity are absent. Water washing of California oil sand was investigated by the U.S. Bureau of Mines, and it was found that soluble salts had to be leached out before separation could be effected (21). Another feature about the Athabasca oil sand is that oil and sand are not adhering to each other in the material as it exists in the deposit and as freshly mined. A film of water separates the oil from the sand grain surfaces. Consequently, it is not a matter of separation but rather one of concentration. Any procedure for treating the oil sand with warm water or hot water results in the oil drawing away from much of the sand and forming oil clots. These oil clots enmesh sand particles. The practical problem is to devise a procedure that will result in the withdrawal of the oil from the sand, while collecting a minimum of mineral matter in the process, into a position from which it can be collected. It must be remembered that the specific gravity of the oil is greater than that of water.

An effective procedure for recovering the oil from the oil sand has been developed by the Research Council of Alberta (7). The first step is to heat and mix the oil sand into a pulp containing 12–15% of water. The pulp is then abruptly flooded with excess water in a manner that involves minimum entrainment of air. The oil collects on the surface of the water as a buoyant froth from where it can be removed by skimming. The froth contains about 5% by weight of mineral matter and about 30–35% of water. A temperature of 185°F. is about the optimum for the pulping and flooding operations.

When the oil sand is mixed and heated to a pulp of 12–15% water content, the oil lies among the sand grains as oil flecks, all of which are small and some of which are very small. The size distribution of the flecks is related to the content of very fine mineral matter in the oil sand. The clay in this fine material is the most potent in effect. Some is required for proper fleck formation but more than enough causes increasing formation of the very fine flecks. On flooding the pulp with water, the coarser

of the oil flecks form bubbles and float to the surface. The very fine flecks do not form bubbles and remain suspended in the water. The gas phase of the froth appears to be water vapor supplemented by air to increase the pressure to that of the atmosphere.

Entrainment of air at the point of flooding the pulp causes a fluffy froth that is loaded with sand particles. At the Bitumount plant a recovery of 90% of the oil as froth was effected. The froth contained 30-35% water and 4-8% mineral matter, dry basis. Other plants where watery pulps were used and where no care was taken to avoid entrainment of air during flooding yielded froths containing about 25% of mineral matter.

No chemical reagents were used in the Bitumount operation. For laboratory studies of the process, soda ash was used in the pulping operation to neutralize acidity which developed in the oil sand during prolonged storage (5).

**Cold-Water Washing.** The Abasand Oils Ltd. plant near McMurray used its version of the hot-water washing method for recovery of oil from the oil sand. Since this method was extravagant of heat, the Mines Branch, Department of Mines and Technical Surveys, Ottawa, studied a procedure for treating the oil sand with cold water (70-80°F.). Comprehensive testing using a continuous pilot plant was done at the Ottawa laboratories (8).

The principles involved in the cold-water treatment are simple. In order to increase the fluidity of the oil content of the oil sand so it will flow readily at room temperatures and to reduce its density below that of water so it will float, a distillate such as kerosene is mixed with the oil sand. Soda ash and a wetting agent are added to the pulp to assist the disengagement of oil and sand. The oil sand so treated is

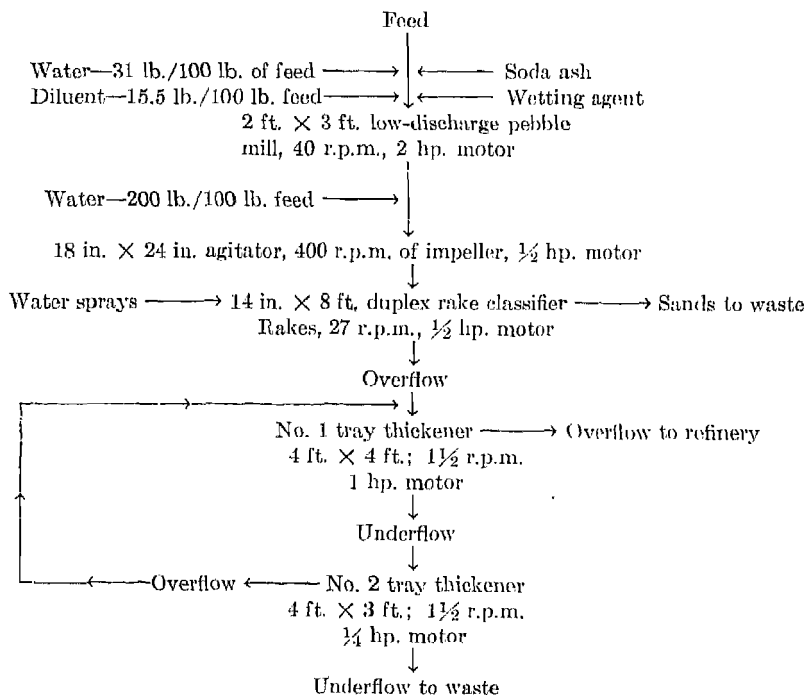


Fig. 2. Flow sheet for the cold-water washing method (27).

agitated in water. The diluted oil floats, as a water-in-oil emulsion, and mineral matter sinks. The oil is collected and then settled to reduce its content of mineral matter and water.

The operation of the process is indicated by a flow sheet (see Figure 2). A net recovery of 95% of the oil in the oil sand treated was obtained. The final diluted oil product contained about 2% mineral matter and 25% water.

**Continuous Retorting.** An obvious approach toward recovery of the oil is to retort the oil sand and to collect the cracked distillate. Little attention was given to this method until the National Research Council, Ottawa, investigated its use as a continuous process through employment of the fluidized solids technique. A laboratory-scale plant was built on the general design of the catalytic cracker. The fluidized solids bed in the reactor was the sand aggregate of the oil sands. Oil sand was fed from the top onto this bed. The oil passed into the gas stream as cracked oil vapors and the carburized sand joined the fluidized bed. The coke formed was burned off the sand in a burner and the hot sand was returned to the reactor. Excess sand was sent to waste through the action of sand level controls. The method worked well and gave a yield of distillates of 85% by volume of the oil in the oil-sand feed. The specific gravity of the combined distillates was 0.960 (16.0 A.P.I.) (16).

An apparent advantage of retorting the oil sand was that a fluid, transportable oil product was obtained directly by one operation. The oil in the oil sand, and as obtained by hot-water washing, is too viscous for handling and would need to be processed by coking or in some other way in a commercial development. The engineering studies involved in the preparation of the Blair report indicated that more favorable costs could be achieved by getting rid of the sand by hot-water washing and then feeding the wet, separated oil to the continuous coking plant than by direct coking of the oil sand. Consequently, the feasibility of feeding wet, separated oil into the fluidized solids bed was examined. It was found that this could be done and that yields and the nature of the distillate were essentially the same as for an oil sand feed (11).

**In Situ Methods.** The methods for recovering oil from the oil sands that have been discussed so far presuppose that the oil sand will be mined for processing. There is considerable scope for this approach to development. Exploration to date has revealed one area of about  $4\frac{1}{2}$  square miles where 125–175 ft. of high-grade oil-sand beds are overlain by 35–75 ft. of sandy overburden. A square mile of good oil-sand beds 100 ft. thick contains about 125 million barrels of oil. A number of favorable areas each of about a square mile in extent have been found. A large volume of oil can be won from the oil-sand formation by open-pit mining and processing.

It is obvious that the great bulk of oil in the McMurray sands cannot be reached by mining operations that are practicable. Overburden conditions are adverse except in restricted areas near the Athabasca river. Also, much of the oil is contained in interbedded oil sand and shale of about 6% oil content as compared to 14% on the average for shale-free oil sand. Some method of *in situ* recovery is needed for gaining possession of the billions of barrels of oil in the main body of the oil-sand formation.

Insight into how *in situ* recovery can be accomplished has been given by the publication by Magnolia Petroleum Co. and by Sinclair Oil and Gas Co. of their work on underground controlled burning in heavy oil reservoirs (13,26). Briefly the method consists in drilling a pattern of holes, on the 5-spot plan for instance, setting fire to the oil sand at half of the holes and collecting oil from the other half. Air under pressure and in controlled amount maintains combustion. The fire front distills the

oil ahead of it and the fuel for the fire is mainly the coke deposited by the destructive distillation. The heat, the diluting action of the distillate formed, and the drive of combustion gases all act to make the heavy reservoir oil fluid and to cause it to move toward the output holes. Recovery of 85% of the oil in the oil sand has been achieved in laboratory burning tests. The method has been tested in actual oil reservoirs with encouraging results.

A test of the possibilities of the burning method in the Athabasca oil sands would be very interesting. Drilling costs would be low because of the shallow depth at which the oil sands lie. A question mark is whether communication through the oil sand of both the shale-free and interbedded varieties can be established and, if so, over what distances. There is vast scope for the method if it can be made to work.

**Oil Evaluation.** The oil-sand oil varies somewhat in regard to specific gravity. The effect of this variation on the composition of the oil is indicated in Table I. The oil samples were obtained by extracting oil sand from various locations with benzene and then removing the benzene by distillation. The oil so recovered was examined by the U.S. Bureau of Mines Hempel distillation method. Although some distillate of the

TABLE I. Hempel Distillation Results for Athabasca Oil-Sand Oils of Various Specific Gravities.

Specific gravity of oil, 25°/25°C.....	1.008	1.013	1.020	1.029
Distillation products, %				
Gas oil.....	23	11	9	7
Nonviscous lubrication distillate.....	6	5	7	5
Medium-viscous lubrication distillate.....	5	9	11	8
Viscous lubrication distillate.....	—	—	—	5
Residuum lubrication distillate.....	66	75	73	75
Properties of residuum:				
Specific gravity, 25°/25°C.....	1.035	1.038	1.046	1.053
Penetration at 25°C., 5 sec., 50 grams.....	too	100	—	—
Penetration at 25°C., 5 sec., 100 grams.....	soft	—	135	53

TABLE II. Laboratory Inspection of Oil-Sand Oil Recovered from Abasand Oils Ltd. Diluted Crude.

A.P.I. gravity at 60°F.....		7.3
Specific gravity at 60°F.....		1.019
Total sulfur, wt. %.....		5.3
Cold test, °F.....		75
Viscosities:		
Kinematic, centistokes at 210°F.....		233
Saybolt Furol at 210°F.....		110
U.O.P. characterization factor.....		11.18
100 ml. distillation:	Atm.	Vacuum (calc. to atm.)
I.b.p. °F.....	456	453
5%.....	543	570
10%.....	590	627
30%.....	670	803
50%.....	703	—
70%.....	709	—
Recovery, %.....	83	32.0
Bottoms, %.....	—	68.0
Coke, wt. %.....	16.6	—



volatility of naphtha was present, its high specific gravity placed it in the category of gas oil (4).

Abasand Oils Ltd. recovered the oil from oil sand by the hot-water washing method. In order to reduce the viscosity and gravity of the oil so that water and mineral matter would settle, an equal volume of a distillate was added to it. A quantity of this diluted crude oil was sent to the Universal Oil Products Co. for study. The diluent was removed by vacuum distillation and the remaining oil was characterized as shown in Table II. Also, it was submitted to a batch coking test with the results shown in Table III (27).

TABLE III. Batch Still Coking of Oil-Sand Oil Recovered from Abasand Oils Ltd. Diluted Crude.

Yields:	Wt. %	Vol. %	
Gas (molecular weight 31.7).....	13.1	—	
Gasoline.....	12.9	17.1	
Gas oil.....	44.9	50.3	
Coke.....	29.6	—	
Product recovery.....	100.5	67.4	
Product properties:	Coke distillate	Gasoline	Gas oil
A.P.I. gravity at 60°F.....	30.9	52.5	24.1
Specific gravity at 60°F.....	0.871	0.770	0.909
Total sulfur, wt. %.....	—	1.84	3.04
Mercaptan sulfur, wt. %.....	—	0.043	—
Bromine number.....	—	69	28
Reid vapor pressure, lb.....	—	3.5	—
Octane no. (motor method).....	—	—	—
Clear.....	—	64.6	—
3 ml. tetracthyl lead/U.S. gal.....	—	69.1	—
Carbon, wt. % (Conradson).....	—	—	0.026
Cetane number.....	—	—	33
Viscosity:			
S.U.S. at 100°F.....	33.9	—	42.4
Kinematic centistokes at 100°F.....	2.35	—	5.03
U.O.P. characterization factor.....	11.22	11.79	11.09
100 ml. distillation:			
I.b.p., °F.....	158	117	444
10%.....	294	194	485
30%.....	449	256	527
50%.....	528	297	563
70%.....	583	330	601
90%.....	647	369	650
End point.....	700	399	704
Inspection of coke:			
Moisture, wt. %.....	0.0		
Ash, wt. %.....	2.8		
Volatile matter, wt. %.....	10.9		
Sulfur, wt. %.....	5.65		

The coker distillate produced by the National Research Council fluidized-solids continuous-coking method is much more fluid than oil-sand oil. It is, nevertheless,

TABLE IV. Inspections of Coker Distillate from Oil-Sand Oil Produced by the Fluidized Solids Continuous Coking Method and of This Distillate after Mild Hydrogenation.

Properties	Coker distillate	Hydrogenated coker distillate
A.P.I. gravity at 60°F.....	16.6	26.2
Specific gravity at 60°F.....	0.963	0.897
Total sulfur, wt. %.....	4.1	0.26
Nitrogen, wt. %.....	0.22	—
Carbon, wt. % (Conradson).....	5.7	1.22
Tar acids, vol. %.....	2.1	
Tar bases, vol. %.....	0.6	
Bromine number.....	45	10
Pour point, °F.....	30	35
Viscosity:		
S.U.S. at 100°F.....	173	55.3
Kinematic centistokes at 100°F.....	37.2	2.38
Distillation (vacuum)		
I.b.p., °F.....	100	108
5%.....	321	250
10%.....	421	330
30%.....	651	530
50%.....	776	681
70%.....	877	751
80%.....	956	—
90%.....	—	857
Recovery, %.....	83	97.5
Bottoms, %.....	17	2.5
% at 400°F. (Hempel).....	8.6	15.0

rather viscous for pipeline transportation. Also, it has a sulfur content of about 4%. Both these unfavorable features can be corrected by mild hydrogenation at 800°F., 1000 p.s.i., and with a hydrogen consumption of about 600 cu.ft. per barrel (30). Inspection data on the N.R.C. coker distillate and on this distillate after mild hydrogenation are given in Table IV (3).

The total distillate from the experimental fluidized solids coking plant was used for hydrogenation. Warren, working at the Mines Branch, Ottawa, found that if the bottom 20% of the distillate, which would be recycled in commercial practice, is eliminated from the total distillate, the remainder hydrogenates much more readily and with reduced hydrogen consumption.

The final product of the sequence of operations proposed in the Blair report for commercial development of the oil sands would be hydrogenated coker distillate. It would consist of about 15% naphtha and 85% of No. 2 furnace oil. Essentially, it would be what is termed "middle distillates" in the oil industry. The production of asphalt from the oil of tar sands and similar materials has been studied (11a). Asphalts can be prepared in high yields from the oil from Athabasca tar sands. These asphalts have properties similar to those from some of the crude oils which are commercially important sources of asphalt.

#### OUTLOOK FOR OIL-SAND DEVELOPMENT

The Athabasca oil sands are a huge source of heavy crude oil that can be tapped when it becomes profitable and expedient to do so. The Blair report indicated that

that time is closer at hand than has been generally supposed. The appearance of important oilfields in Alberta has probably advanced rather than retarded oil-sand development by necessitating the installing of facilities, notably pipelines, for extensive oil production.

### U.S. Deposits

Of the several outcropping deposits of oil-soaked sands in the United States, the largest and richest accumulations are in California and Utah. Substantial deposits also are found in Kentucky, Oklahoma, and Texas. The California deposits occur principally in the immediate region of the coast range mountains. Those near the cities of Santa Cruz and San Luis Obispo and the town of Sisquoc are the largest and together have been estimated by the U.S. Geological Survey to contain in the neighborhood of 200,000,000 barrels of oil. The Utah deposits are near Vernal in the Uintah Basin and near the coal-mining town of Sunnyside on the southern edge of the Uintah Basin. The latter deposits lie at elevations between 9000 and 10,000 feet near the top of Book Cliffs. A conservative estimate by the Geological Survey indicates that the Vernal deposit contains 1,150,000,000 barrels of bitumen. The Geological Survey has also estimated that the measured and indicated bituminous sandstone of the Sunnyside deposit contains 728,000,000 barrels of bitumen.

**Hot-Water Separation Tests.** Hot-water separation tests have been run in the San Francisco laboratory of the Bureau of Mines on quarry samples of oil sands from the Edna deposits near San Luis Obispo, California, and from the Vernal and Sunnyside, Utah, deposits (21). The fundamental principles of separating bitumen from the Athabasca oil sands were applied in treating the foregoing sandstones. The separation of bitumen from bituminous sandstone by water is based on the well-known phenomenon that water, because of its preferential wettability for silica, will displace crude oil from quartz-sand grains and other siliceous particles. Certain alkaline solutions are more effective than plain water as a displacing medium, and virtually complete displacement of the bitumen readily takes place when the water is alkaline enough to neutralize any acidity that may be present in the bituminous sandstone.

The presence of soluble mineral salts in the Edna sandstones, consisting largely of iron and calcium sulfates with some sodium and aluminum sulfates, made it necessary to water-wash the sandstones to remove these troublesome impurities. Hydrolysis of the ferrous sulfate made the bituminous sandstone distinctly acid, which precluded the separation of any bitumen in the washing process. Unless removed, these salts reacted with the alkaline reagents in the pulper and formed gelatinous iron and calcium hydroxides, which were precipitated in the separation cells. They prevented the flotation of fine particles of bitumen and caused excessive quantities of bitumen to be lost to the slimes and sand tailings and the percentage recovery to be reduced.

The results of the separation tests demonstrated that neutralization of the acidity of the charge with sodium silicate or sodium carbonate solutions is a fundamental requirement for complete displacement of the bitumen from the sand grains. The addition of a light-gravity fuel-oil diluent facilitated displacement of the bitumen. Removal of the acid iron salts greatly reduces the quantity of alkaline reagents required to neutralize acidity in pulping the bituminous sandstones. The most satisfactory diluent to use in pulping the sandstone and in diluting the oil froth to facilitate settling of the water, sand, and silt is one containing substantial quantities of aromatic compounds.

Careful control of the pH of the treating system also is an important factor in processing the Edna sandstones. Best results, as reflected by complete displacement of the bitumen from the sand grains in the pulper, rapid separation of the oil froth in the flotation cells, and effective settling of the water and silt from the end product were obtained when the alkalinity of the system was maintained at pH 8. Under carefully controlled operating conditions a maximum recovery of 95% of the bitumen in the Edna sandstones can be expected.

The separation tests showed that the Vernal and Sunnyside bituminous sandstones also respond to treatment by the hot-water method of separation. The bitumen in the Vernal sandstone was extracted more readily by the action of hot water than was the Edna bitumen, which greatly simplified plant operation. The Vernal sandstone contains no water-soluble iron compounds, such as were found in the Edna sandstone, and, therefore, required no preliminary water washing. Recovery of bitumen from the Vernal sandstone was about 96%.

In contrast to the softness of Edna and Vernal sandstones, the Sunnyside sandstone is an extremely hard asphalt rock that must be crushed to small size to facilitate complete disintegration and displacement of the bitumen from the sand grains in pulping. The disintegrated sand was fine and contained a high percentage of silt, which increased the loss of bitumen to the tailings discharged from the plant. About 90% of the original bitumen in the Sunnyside sandstone was recovered.

### Bibliography

- (1) Adkins, W. E., *World Petroleum*, **20**, 40-45 (1949).
- (2) Ball, M. W., *Trans. Can. Inst. Mining Met.*, **44**, 58-91 (1941).
- (3) Blair, S. M., *Report on the Alberta Bituminous Sands*, Government of the province of Alberta, Edmonton, 1950.
- (4) Clark, K. A., and Blair, S. M., *Sci. Ind. Research Council Alberta (Can.), Rept.*, No. 18, 67 (1927).
- (5) Clark, K. A., and Pasternack, D. S., *Ind. Eng. Chem.*, **24**, 1410-60 (1932).
- (6) Clark, K. A., *Can. J. Research*, **F22**, 174-80 (1944).
- (7) Clark, K. A., and Pasternack, D. S., *Research Council Alberta (Can.), Rept.*, No. 53 (1949).
- (8) Djingheuzian, L. E., *Proceedings, Athabasca Oil Sands Conference*, Government of the province of Alberta, Edmonton, 1951, pp. 185-99.
- (9) Eldridge, G. H., *U.S. Geol. Survey Ann. Rept.*, **1900-01**, Pt. Ib, pp. 365-452.
- (10) Ellis, S. C., Bituminous sands of northern Alberta. *Can. Dept. Mines and Resources, Mines Branch*, No. 632, 1926.
- (11) Hodgson, G. W., Matchen, B., Peterson, W. S., and Gishler, P. E., *Ind. Eng. Chem.*, **44**, 1492 (1952).
- (11a) Hubbard, R. L., and Stanfield, K. E., *U.S. Bur. Mines, Rept. Invest.*, **4523** (1949).
- (12) Hume, G. S., *Trans. Can. Inst. Mining Met.*, **50**, 298 (1947).
- (13) Kuhn, C. S., and Koch, R. L., *Oil Gas J.*, **52**, No. 14, 92 (1953).
- (14) McConnell, R. G., *Geol. Survey Can.*, V, Pt. I, Sect. D, 64 (1891).
- (15) Pasternack, D. S., and Clark, K. A., *Research Council Alberta (Can.), Rept.*, No. 58 (1951).
- (16) Peterson, W. S., and Gishler, P. E., *Proceedings, Athabasca Oil Sands Conference*, Government of the province of Alberta, Edmonton, 1951, p. 207.
- (17) Platz, H., *Petroleum*, **33**, No. 43, 12 (1937).
- (18) Rice, G. S., *U.S. Bur. Mines, Bull.*, **351** (1932).
- (19) Russell, L. S., *Trans. Roy. Soc. Can.*, **Sect. IV**, **26**, 37 (1932).
- (20) Scott, J., Collins, G. A., and Hodgson, G. W., *Trans. Can. Inst. Mining Met.*, **57**, 34 (1954).
- (21) Shea, G. B., and Higgins, R. V., *U.S. Bur. Mines, Rept. Invest.* **4246** (1948); 4871 (1952).
- (22) Staff, *Geol. Survey Can., Summary Rept.*, **10**, 18A (1897).
- (23) Staff, *Geol. Survey Can., Summary Rept.*, **11**, 22A (1898).
- (24) Staff, *Can. Dept. Mines and Tech. Surveys*, No. 826 (1949).

- (25) Staff, *Proceedings, Athabasca Oil Sands Conference*, Government of the province of Alberta, Edmonton, 1951.
- (26) Staff, *Oil Gas J.*, **52**, No. 16, 111 (1953).
- (27) Sterba, M. J., *Proceedings, Athabasca Oil Sands Conference*, Government of the province of Alberta, Edmonton, 1951, p. 257.
- (28) Tanner, N. E., *Proceedings, Athabasca Oil Sands Conference*, Government of the province of Alberta, Edmonton, 1951, p. 169.
- (29) Ward, S. H., and Clark, K. A., *Research Council Alberta (Can.), Rept.*, No. 57 (1950).
- (30) Warren, T. E., Booth, F. L., Carson, R. E., and Bowles, K. W., *Proceedings, Athabasca Oil Sands Conference*, Government of the province of Alberta, Edmonton, 1951, pp. 289-305.

K. A. CLARK

G. B. SHEA (U.S. Deposits)

**TARTAR EMETIC**,  $\text{KSbC}_4\text{H}_4\text{O}_7 \cdot \frac{1}{2}\text{H}_2\text{O}$ . See *Anthelmintics*, Vol. 1, p. 937; *Antimony preparations*, Vol. 2, p. 65; *Emetics and expectorants*, Vol. 5, p. 680; *Tartaric acid*.

## TARTARIC ACID

Tartaric acid of commerce, U.S.P. XIV, is the dextro form of 2,3-dihydroxysuccinic acid (I),  $\text{C}_4\text{H}_6\text{O}_4$ , formula weight 150.06. *dextro*-Tartaric acid ((+)-tartaric acid) has been known since antiquity in the form of its acid potassium salt, which occurs in grapes. In the fermentation of grape juice to wine, the salt deposits in the fermentation vessels. The free crystallized tartaric acid was first obtained from such fermentation residues by Scheele in 1769.

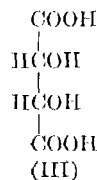
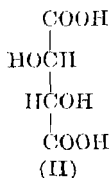
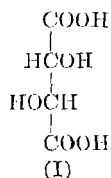
## Properties

**Physical Properties.** *dextro*-Tartaric acid, when crystallized from aqueous solutions above 5°C., is obtained in the anhydrous form. Below 5°C., it forms a monohydrate, unstable even at room temperature. The anhydrous crystals belong to the monoclinic system and melt at 169-70°C.; specific gravity at 20°C. is 1.76. The optical rotation of an aqueous solution varies with the concentration: for a concentration *c* between 20% and 50%  $[\alpha]_D^{20} = 15.050^\circ - 0.1535 c$ . The solid crystals are levorotatory,  $\alpha_D$  of a 1-cm. layer being  $-114^\circ$ . Tartaric acid is a strong organic acid with the first dissociation constant  $8.96 \times 10^{-4}$  and the second  $7.46 \times 10^{-5}$ . The solubility of *dextro*-tartaric acid is given in Table I. 100 grams absolute ethyl alcohol dissolve 20.4 grams tartaric acid at 18°C.; 100 grams ether dissolve 0.30 gram tartaric acid at 18°C.

TABLE I. Solubility of *dextro*-Tartaric Acid.

Temp., °C.	Soly., g./100 g. H <sub>2</sub> O	Temp., °C.	Soly., g./100 g. H <sub>2</sub> O	Temp., °C.	Soly., g./100 g. H <sub>2</sub> O
0.....	115	35.....	166	70.....	244
5.....	120	40.....	176	75.....	258
10.....	125	45.....	185	80.....	273
15.....	132	50.....	195	85.....	290
20.....	139	55.....	206	90.....	307
25.....	147	60.....	218	95.....	325
30.....	156	65.....	230	100.....	343

**Isomerism.** Tartaric acid can be obtained in four forms. Formulas (I) and (II) represent *dextro*- and *levo*-tartaric acid, the prefixes referring to the direction of rotation of the plane of polarization of polarized light; (III) is *meso*-tartaric acid, which is inactive by "internal compensation." In addition there is the racemic form, racemic acid, which is an equimolecular mixture of (I) and (II).



The precise stereochemical nomenclature of the active tartaric acids can be confusing, because, since both ends of the molecule are alike, it is possible to take either the carbon-2 or the -3 as the basis for designating the configuration. Thus, (I) is *L*-tartaric acid with reference to the lower of the two intermediate carbon atoms as written, that is, the 3 atom numbering from the top, but it is *D*-tartaric acid with reference to the 2 atom. The American Chemical Society Committee on Nomenclature has suggested (1) that, in cases where an ambiguity of this kind exists, the number of the reference carbon atom be inserted: thus *dextro*-tartaric acid (I) can be referred to as *D*(2)(*R*)-tartaric acid or as *L*(3)(*R*)-tartaric acid. The *R* indicates relative configuration.

It has been shown by x-ray structure analysis (17) that the conventional (relative) structure (I) for *dextro*-tartaric acid, in which the first hydroxyl from the bottom appears at the left (in the conventional manner of stereochemical representation), actually does conform to the true structure.

*dextro*-Tartaric acid occurs in numerous plants and fruits, although it is not as widely distributed as citric or *L*-malic acid. The only commercial source is the residues from the wine industry.

*levo*-Tartaric acid has been found in the fruit and leaves of *Bauhinia reticulata*, a tree native to the French Sudan (20). Like the *dextro* acid, it forms anhydrous monoclinic crystals.

*Racemic acid* is not a primary product of plant processes, but is readily formed from the *dextro* acid by heating with strong alkali or strong acid or by heat alone. As the classical example of an optically inactive compound originating from the combinations of molar proportions of the *dextro* and *levo* isomers, it is of considerable historical interest. The methods by which such racemic compounds can be separated into the optically active modifications were devised by Pasteur and first applied to racemic acid. Racemic acid crystallizes as the hydrate  $(\text{C}_4\text{H}_6\text{O}_6)_2 \cdot 2\text{H}_2\text{O}$  in triclinic prisms. It becomes anhydrous on drying at  $110^\circ\text{C}$ . and melts at  $205^\circ\text{C}$ . Calcium racemate,  $(\text{C}_4\text{H}_4\text{O}_6\text{Ca})_2 \cdot 8\text{H}_2\text{O}$ , is still less soluble in water than calcium tartrate: thus, a dilute racemic acid solution is precipitated by a saturated calcium sulfate solution while active tartaric acid is not.

*meso*-Tartaric acid is not found in nature. It is obtainable from the other isomers by prolonged boiling with caustic alkali. The free acid crystallizes as a monohydrate,  $\text{C}_4\text{H}_6\text{O}_6 \cdot \text{H}_2\text{O}$ , in monoclinic prisms. On drying at  $110^\circ\text{C}$ ., it becomes anhydrous and melts at  $159$ – $60^\circ\text{C}$ .

Table II compares the physical properties of the isomers.

TABLE II. Physical Constants of Tartaric Acids.

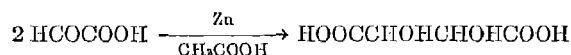
	Dextro	Levo	Racemic	Meso
M.p., °C. (anhydrous)	169-70	169-70	205-6	159-60
Soly. in water, at 20°C., g./100 g. H <sub>2</sub> O	139	139	20.6	125
Soly. of acid potassium salt, at 25°C., g./100 g. H <sub>2</sub> O	0.84	0.84	0.72	16.7
Moles of water in hydrate of calcium salt	4	4	8	3

**Synthesis.** All of the isomers have been prepared synthetically. Optically active acids, dextro as well as levo, can be obtained by oxidation of suitable carbohydrates (8,22), but the recoveries are unsatisfactory because of the simultaneous formation of many by-products. *dextro*-Tartaric acid of high optical and chemical purity can be made by chemical (21) or biological oxidation (24) of 5-ketogluconic acid. However, neither method is in use at present on an industrial scale. Racemic and meso acids may also be prepared by purely synthetic procedures. Examples are:

(1) Application of the cyanohydrin (*q.v.*) reaction to glyoxal leads to the formation of both racemic and *meso*-tartaric acids:



(2) Reduction of glyoxylic acid with zinc dust in acetic acid solution yields racemic acid:



(3) Hydroxylation of fumaric acid or maleic acid ( $\text{HOOCCH}=\text{CHCOOH}$ ) can be directed to form primarily either *meso*-tartaric or racemic acid, depending on the hydroxylation agent and the catalyst used (14). An efficient method for the manufacture of racemic acid from maleic anhydride and hydrogen peroxide using a tungstic oxide catalyst has been published recently (6).

**Reactions.** When free *dextro*-tartaric acid is heated above its melting point (170°C.), amorphous anhydrides are formed which on boiling with water regenerate the acid. Further heating causes simultaneous formation of pyruvic acid,  $\text{CH}_3\text{COCOOH}$ , and pyrotartaric acid,  $\text{HOOCCH}_2\text{CH}(\text{CH}_3)\text{COOH}$ , and finally a black, charred residue. Hydrogen peroxide in the presence of ferrous salt forms dihydroxymaleic acid,  $\text{HOCCOH}=\text{COHCOOH}$ . Nitrating acid yields a dinitro ester which on hydrolysis is converted to dihydroxytartaric acid,  $\text{HOCC}(\text{OH})_2\text{C}(\text{OH})_2\text{COOH}$ . The latter goes to tartronic acid,  $\text{HOCH}(\text{COOH})_2$ , on oxidation with nitric acid. Acetyl chloride or acetic anhydride forms diacetyltartaric anhydride,  $\text{OC}\cdot\text{CH}(\text{OOCCH}_3)\cdot\text{CH}(\text{OOCCH}_3)\cdot\text{CO}$ , readily hydrolyzable to diacetyltartaric acid.

Tartaric acid is reduced stepwise with concentrated hydriodic acid, first to *D*-malic acid,  $\text{HOOCCHOHCH}_2\text{COOH}$ , and then to succinic acid,  $\text{COOH}(\text{CH}_2)_2\text{COOH}$ . Ammoniacal silver solution is reduced with the formation of a silver mirror. The hydroxyl groups enable the acid to prevent the precipitation by bases of numerous metal salts, including those of aluminum, iron, copper, and lead. In other words, tartaric acid acts as a complexing agent.

**Salts and Esters.** Tartaric acid forms stable acid (monobasic) and neutral (dibasic) salts, also acid and neutral esters. The salts of commercial importance are: *Acid potassium tartrate* (potassium hydrogen tartrate, cream of tartar, potassium bitartrate, N.F. IX),  $\text{KHC}_4\text{H}_4\text{O}_6$ , formula weight 188.2, solubility, g./100 ml. water: 0.6 at 20°C., 6.1 at 100°C. *Potassium sodium tartrate*, N.F. IX (Rochelle salt),  $\text{KNaC}_4\text{H}_4\text{O}_6 \cdot 4\text{H}_2\text{O}$ , formula weight 282.2, water of crystallization 25.5%, solubility, g./100 ml. water: 26 at 26°C., 66 at 100°C. *Potassium antimony tartrate* (antimony potassium tartrate, U.S.P. XIV, tartar emetic),  $\text{K}(\text{SbOH}_2)\text{C}_4\text{H}_4\text{O}_6 \cdot \frac{1}{2}\text{H}_2\text{O}$ , formula weight 333.9, water of crystallization 2.7%, solubility, g./100 ml. water: 8.7 at 25°C., 35.7 at 100°C. (See also *Antimony preparations*, Vol. 2, p. 65.) *Calcium tartrate*,  $\text{CaC}_4\text{H}_4\text{O}_6 \cdot 4\text{H}_2\text{O}$ , is the usual intermediate in the commercial production of tartaric acid. The neutral strontium and barium salts are similar compounds of low solubility in water. The neutral heavy-metal salts are water-insoluble, but soluble in excess of neutral or alkaline solutions of alkali tartrates.

The neutral esters of the lower aliphatic alcohols, formed by the usual esterification methods, are liquids or low-melting solids. Their properties are shown in Table III. See also Vol. 5, p. 832.

TABLE III. Diesters of *dextro*-Tartaric Acid.

Ester	M.p., °C.	B.p., °C.	Sp.gr.	$[\alpha]_D^{25}$
Methyl	48 and 61.5	165–66 <sub>11.5</sub>	1.2903 <sup>32</sup>	+6.15 <sup>30</sup>
Ethyl	17	155–56 <sub>15</sub>	1.2112 <sup>18</sup>	+7.48 <sup>20</sup>
<i>n</i> -Propyl	Liquid	174 <sub>12</sub>	1.1361 <sup>18</sup>	+11.7 <sup>14</sup>
Isopropyl	Liquid	157–58 <sub>16</sub>	1.1274 <sup>18</sup>	+15.7 <sup>14</sup>
<i>n</i> -Butyl	22	186 <sub>14</sub>	1.0886 <sup>18</sup>	+10.3 <sup>10</sup>
Isobutyl	70	195 <sub>13</sub>	1.0213 <sup>30</sup>	+19.9 <sup>30</sup>

**Analysis.** When a few milligrams of tartaric acid are heated in a steam bath with 2 ml. concentrated sulfuric acid containing 0.5% pyrogallol, an intense violet color is produced. A similar color is developed with resorcinol and sulfuric acid when heated to 130°C. These color reactions are not given by citric or malic acid. Paper chromatography is the best method for identification and approximate quantitative estimation in the presence of other organic acids (15,17). The usual quantitative determination is by precipitation of the acid potassium salt with an excess of potassium acetate or citrate and acetic acid in dilute alcohol and subsequent titration of the precipitate. The commercial analysis for tartars, which is based on this procedure, is known as the *Goldenberg analysis* (2). Polarimetric methods whereby advantage is taken of the greatly enhanced rotatory power obtained in the presence of uranyl acetate or sodium molybdate are also in use (5).

**Physiological Properties.** Tartaric acid unlike citric and other fruit acids is not metabolized in the human system. Upon oral administration, a very small portion is oxidized to carbon dioxide, 20% is found in urine, and none is left in feces, owing to bacterial destruction in the intestines. When it is given parenterally, excretion is quantitative in the urine after 10 hours (11). It is not well absorbed in the gastrointestinal tract but exerts a cathartic effect. Orally, the toxicity of the tartrate ion is very low due to lack of absorption. Parenteral injection in quantity immobilizes the blood calcium and endangers heart action.



### Manufacture of the Acid and Its Salts (3,9,10,19a)

The raw materials available for the manufacture of tartaric acid and tartrates are by-products of wine making. Crude tartars are recoverable from the following sources. See also *Wines*.

(1) The press cakes from the grape juice, unfermented or partly fermented (*marcs* or *pomace*). The residues are boiled up with water, and alcohol if present is distilled off. The hot mash is settled, decanted, and the clear liquor cooled to crystallize. The recovered high-test crude cream of tartar, *vinaccia*, has an 85–90% cream of tartar content. A continuous process for the recovery of calcium tartrate from winery pomace is in operation in California (13).

(2) *Lees* are the dried slimy sediments in the wine fermentation vats, consisting of yeast cells, pectinous substances, and tartars. Italian lees contain 20–30% total tartaric acid of which 5–6% is calcium tartrate. French lees contain 16–22% total tartrate, Spanish 20–35%, and Dalmatian, Greek, and Turkish 30–42%.

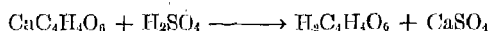
(3) The crystalline crusts formed in the vats in the secondary fermentation period are known as *argols*. These products contain more than 40% total tartaric acid; they are high in potassium bitartrate and low in calcium. *Limo* or *sablons* are argols, high in calcium, originating from Italy.

It is usually advantageous to combine the manufacture of tartaric acid, cream of tartar, and Rochelle salt in one plant. This permits the most favorable disposition of the mother liquors from the three processes. Some plants include a system for potassium salt recovery.

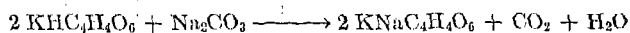
The chemical reactions involved are as follows: Formation of calcium tartrate from crude potassium acid tartrate:



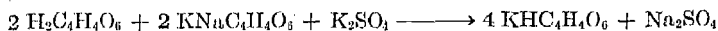
formation of tartaric acid from calcium tartrate:



formation of Rochelle salt from argols:



formation of cream of tartar from tartaric acid and Rochelle salt liquors:



This simple recovery scheme is complicated by inorganic and organic impurities. One of the greatest difficulties is the poor filterability of the crude tartar solutions. Mechanical filter aids such as diatomite are quite ineffective, as is coagulation by chemical means such as treatment with formaldehyde. Wet autoclaving at 50–60 lb. pressure or dry roasting at 150–160°C. of the crude tartar is used to obtain satisfactory filtration.

**Preparation of Calcium Tartrate.** The oldest procedure is the *decantation process*, in which fresh wet lees or finely ground dry lees are treated with sufficient hydrochloric acid to dissolve all tartrates. The acidified magma is diluted with sufficient water to obtain at least 50% supernatant solution after settling. The acid liquor is drawn off and the insolubles are washed by repeated suspension in water and decantation. The combined extracts are neutralized with ground limestone or hydrated lime, leaving the end reaction slightly acid to litmus to reduce coprecipitation of the phosphates of iron

and aluminum. The process requires only wooden vats and simple gravity filters, but simplicity of the equipment does not compensate for the large volumes of solution required and consequent solubility losses.

Tartar recovery from winery still slops (still residues) may be accomplished by *exchange adsorption* on an ion exchanger in the chloride form. Common salt solution serves as the regenerant. Concentration of the tartrate in solution is increased 15–18 times over that in the original slop. High-purity calcium tartrate is the final product (12).

In the *neutral pressure process*, the ground tartars are suspended in a wooden tank with three parts of water, heated to boiling with direct steam, and then nearly neutralized with a slurry of hydrated lime. The magma is pumped into an iron autoclave equipped with agitator and heated with direct steam to 50 lb. pressure for two to three hours. After releasing the pressure, the mass is dropped into an open iron tank fitted with an iron gate stirrer and a cooling jacket. After cooling to 30°C., the batch is treated with calcium chloride until there is about a 5% excess over the amount calculated for the original acidity of the batch, then the cooling is continued to the temperature of the cooling water available. The slurry is filtered and washed in an iron filter press. The press cake must be strongly acidified with sulfuric acid without delay, since the neutral tartrates become easily infected with bacteria which, once established, can cause severe losses of tartrate in the course of a few hours. It is good plant practice to keep all equipment scrupulously clean at all times and sterilize, with sulfur dioxide or formaldehyde, tanks, pipelines, pumps, and press whenever the plant is idle even for a short time.

**Roasting Process.** Older plants that practiced roasting of argols roasted the material in rotating cylinders which were heated directly by fire gases. Local overheating resulting in destruction of tartars was unavoidable and a number of European plants abandoned the process in favor of the wet pressure cook. However, satisfactory temperature control is obtainable by indirect heating through pressure steam or by a high-boiling fluid such as Dowtherm, the eutectic mixture of diphenyl and diphenyl oxide. The roaster consists of a horizontal cylinder fitted with a horizontally mounted agitator with numerous blades. It is surrounded by a heating jacket through which the heat-transfer agent is circulated. Automatic controls maintain the desired temperature. The roasters take a charge of 5,000–10,000 lb. of crude tartars. Before entering the roaster, the crude material is ground in a mill with swing beaters similar to a Gruendler mill to pass a 20–30 mesh screen. Roasting time is from 2 to 6 hours at 155–165°C. depending on the crude. The roasted product is transferred by means of a screw conveyor to a wooden precipitation tank provided with a cooling coil. Hydrated lime slurry is added rapidly until neutrality to litmus is reached. A slurry of precipitated calcium sulfate is added until a 20% excess is present. After cooling to 30°C., the reaction mixture is filtered on a large rotary filter and washed with cold water. The filtrate from this press goes to storage tanks for subsequent evaporation to potassium sulfate crystals. The cake from the rotary press is repulped and re-washed on a second rotary press. The filtrate from this second press goes to the sewer.

**Recovery of Potassium Sulfate.** The filtrate and wash from the first rotary press as collected in the storage tanks averages 5°Bé. It is treated with sodium carbonate to precipitate calcium and then sent through an iron filter press. The press cake is discarded. The clear filtrate goes to a triple-effect pressure evaporator maintained at 60 lb. pressure in the first effect, 45 lb. in the second effect, and 3–15 lb. in the third

effect. The crystallized potassium sulfate is collected on drain boxes where it is washed with cold water. The salt is dried in a current of hot air.

**Decomposition of Calcium Tartrate.** The washed press cake is slurried up with weak wash water from a previous acid charge and acidified with cold 70% sulfuric acid to a pH of 0.8 at 15°Bé. The batch is filtered on large wooden vacuum filter boxes and the calcium sulfate – pomace cake washed with cold water. The wash liquors down to 3°Bé. are combined with the strong liquor, the weaker washings being used for make-up of the next charge. The strong liquor is drawn into an antimony-lead vacuum pan equipped with nickel heating tubes that are supplied with exhaust steam at 3–5 lb. pressure. The pan is served by a steam evacuator and a tubular copper condenser. The tartaric acid liquor is concentrated to 31–32°Bé. at 70°C. and then filtered free of calcium sulfate on a filter box, using porous stoneware as the filter medium. The clear filtrate is drawn into a copper vacuum still equipped with copper heating coils and evaporated until a very heavy magma of crystals is obtained. The charge is then dropped into lead-lined stirred granulators and, while still warm, is freed of mother liquor in centrifuges. The first crop represents a 65% yield. The mother liquor from the first crystallization is filtered and boiled down *in vacuo* to obtain a second crop. Similarly, the mother liquor from the second crop yields a third crystallization, which is of poorer quality. If the ash is over 1%, the material is redissolved in a subsequent fresh tartaric acid charge. The mother liquor from the third crystallization becomes “old liquor.” The tartaric acid remaining in the old liquor is recovered either as calcium tartrate (10) or as cream of tartar (9). Probably every tartaric acid plant has its own variation for the most favorable recovery. Troublesome impurities are salts of aluminum, iron, copper, and lead. Lead and copper are best eliminated as sulfides, and iron as ferrocyanide. Aluminum can be considerably reduced by treating the warm old liquor with potassium sulfate; on cooling with agitation, potassium alum will crystallize, and is separated by centrifugation.

**Finished Tartaric Acid.** The first and second crude crystallizations are dissolved in wooden tanks with wooden stirrers. An open steam line is used for heating. Enough water is used to make a 30°Bé. solution at 50°C. Sulfate is removed with barium carbonate and iron with calcium ferrocyanide; decolorizing charcoal is also added at this point. Proper adjustments are made by laboratory tests. The liquor is filtered through a wooden plate-and-frame press and sent to Monel metal storage tanks. Evaporation to crystallization is done in a Monel metal vacuum pan fitted with a single-stage evacuator and a brass tubular condenser. For the production of larger crystals the liquor is evaporated to 39–40°Bé. under vacuum and then run into crystal pots. These are conical stainless steel or Monel metal pots of 50-gallon capacity. On slow cooling, crystallization is complete in 5 days. The pots are easily emptied onto a Monel metal sheet, and after draining the crystals are crushed by a rotary pronged crusher, centrifuged, and washed with a little cold water. The yield is about 170 lb. of washed crystals per pot.

The granular finished product is made in the same Monel metal vacuum pan. The granular is dropped from the pan at 70°C., centrifuged at that temperature, and washed with pure saturated tartaric acid solution. The mother liquor can be used a number of times before it is returned to the crude crystallization liquor. The granular product is dried in a rotary drum constructed of aluminum or stainless steel. Hot air (70°C.) is drawn through the drum by a fan at the feed end and the discharge is through a dust collector. The product is sifted through a set of screens, for

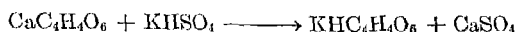
example top 16 mesh, second 30 mesh, third 74 mesh. Tartaric acid powder is made with a Raymond impact pulverizer or similar equipment provided with air separation. Tartaric acid produced by the process described meets the U.S.P. specifications and is shipped in 25-, 50-, 100-, 230-, and 250-lb. drums in the form of crystals, granular of various screening characteristics, or powder. Prices quoted in early 1954 were 37½¢ in carload lots and 38½¢ in 250-lb. drums.

**Manufacture of Rochelle Salt and Cream of Tartar (4).** Argols are blended to assay 75–85% bitartrate and not over 6% calcium tartrate. These are roasted for 5 hours at 160–165°C. The charge is then dropped into a Monel metal tank which contains weak wash liquor from a previous charge. Soda ash in slight excess over the calculated amount is added as rapidly as possible while the batch is stirred and the temperature brought to 80°C. When evolution of carbon dioxide has ceased, calcium in solution is reduced to a minimum by addition of potassium oxalate with repeated testing of filtered samples. The filtrate should be about 38°Bé. The charge is filtered through a 48-in. wooden plate-and-frame press and washed until the washings are 30°Bé. These strong liquors are collected separately in a stainless steel cook tank for the manufacture of Rochelle salt. The wash waters to 18°Bé. are collected for the manufacture of cream of tartar (see below). The wash waters from 18 to 0°Bé. are used for the next argol neutralization. The Rochelle liquor is evaporated to 41½°Bé. at 100°C. A check titration is made using phenolphthalein as indicator and adjustment is made with either soda ash or cream of tartar. Sufficient sodium sulfide is added to remove iron, and decolorizing charcoal to remove coloring matters. The charge is filtered through a stainless steel filter press and run into stainless steel granulators equipped with cooling jacket and cooling coils. When cold, the Rochelle salt is centrifuged, washed with water in the centrifuge, and dried in a rotating drum by a stream of warm air. The dried product is screened and, if required, milled in a way similar to that described for tartaric acid. If suitable argols, high in bitartrate and low in calcium tartrate, are not available, it is preferable to make up the Rochelle salt cook either partly or entirely with purified cream of tartar. Rochelle salt is usually marketed as powder or as fine granular in 25-, 50-, 100-, 225-, and 250-lb. drums. Prices quoted during the second quarter of 1954 were 33–33½¢ per pound in carload lots.

**Cream of Tartar.** Cream of tartar is usually produced by combining tartaric acid solutions available from the manufacture of tartaric acid with Rochelle salt solution derived from suitable crude potassium bitartrate such as high-grade argols or recovered cream of tartar. Potassium sulfate is added on the basis of 1 mole  $K_2SO_4$  for 2 moles of free tartaric acid introduced. The acid liquor is heated to 60°C. and treated with decolorizing carbon. Heavy metals are removed by conventional means. Filtration is done through a wooden plate-and-frame press, the filtrate being received in enamelled storage tanks. The neutral Rochelle liquor is freed of calcium and heavy metals, treated with decolorizing carbon, and filtered and the filtrate collected in Monel or stainless steel storage tanks. Hot neutral and acid liquors are run simultaneously into enamelled or Monel granulators fitted with cooling coils. During the precipitation the pH is held between 3.2 and 3.5. The precipitated cream of tartar is centrifuged and washed thoroughly with water, then dried on a rotating drum by a stream of hot air, and milled in an impact pulverizer. The cream of tartar remaining in the mother liquor is recovered as calcium tartrate.

**Water-Cook Process.** Small plants still favor the recovery of cream of tartar by

recrystallization from water. For coagulation of organic material, roasting is desirable. French practice prescribes a preliminary treatment with formaldehyde whereby it is said to be possible to reduce the roasting temperature to 140°C. At such low temperature, roasting can safely be done with direct heat from fire gases. The roasted charge is boiled in a wooden tank with sufficient water to make a 6% cream of tartar solution. Calcium tartrate present is converted to cream of tartar by addition of potassium bisulfate which reacts in accordance with the equation:



The cook is settled while near 100°C., and the supernatant liquor decanted. The pomace and calcium sulfate sediment are put through a preheated wooden filter press. The cream of tartar is crystallized by agitation and cooling to room temperature. The mother liquor, which can be re-used repeatedly, is finally withdrawn and the remaining tartrate recovered by precipitation as calcium tartrate in the usual manner. Some tartrate remains in the pomace and is recoverable by re-extraction with hot mother liquor.

*Sulfur Dioxide Process.* The principle of the process is to saturate a water suspension of argols with sulfur dioxide, whereby cream of tartar as well as calcium tartrate are dissolved to an approximate 7% solution. The pomace can then be removed on a pressure filter. On boiling the filtrate or applying vacuum, sulfur dioxide is driven off, thus reprecipitating the tartars in purified form. Most of the sulfur dioxide can be recovered by absorption in a new batch. The calcium tartrate present in the raw material is preferably converted to cream of tartar by the addition of an equivalent quantity of potassium acid oxalate or potassium acid sulfate previous to the treatment with sulfur dioxide.

*Aluminum Chloride Process.* This unusual procedure utilizes the high solubility of cream of tartar in hot concentrated aluminum chloride solution combined with a favorable solubility differential on cooling. The process is only recommended for argols with over 80% bitartrate, in order to avoid too frequent a regeneration of the mother liquor. Moreover, the process must be carried out in costly enamelled equipment because of the corrosive action of aluminum chloride (7).

*Other Processes.* Obviously, cream of tartar can be produced directly from the argol soda ash cook without diverting any part of it to the manufacture of Rochelle salt. In this case, the whole batch is neutralized with sufficient acid liquor as described.

Cream of tartar is usually packed as powder in 25-, 50-, 100-, and 250-lb. drums. Price quoted in the second quarter of 1954 for the domestic product in 100- and 250-lb. drums was 33¢ in 500-lb. to carload lots.

**Tartar Emetic.** In the manufacture of tartar emetic, the plant equipment is best constructed throughout of stainless steel. The reaction tank, fitted with heating coils and an agitator, is charged with 500 gal. of water, and while heating and stirring, 3400 lb. of antimony oxide,  $\text{Sb}_2\text{O}_3$ , and 4300 lb. of potassium bitartrate are added simultaneously. When the raw materials are in, the reaction is continued at 100°C. for at least four hours. For good reactivity, antimony oxide made by wet precipitation should be used, the oxide made by sublimation being unsuitable. The reaction mixture is then diluted to 24–25°Bé. at 100°C., circulated through a filter press pre-coated with diatomite until clear, and then collected in jacketed granulators, where it is

cooled to 25°C. and allowed to crystallize. The crystals are centrifuged and washed free of mother liquor with cold water. The material is air-dried and milled to an 80-mesh powder. The mother liquor can be re-used several times. Accumulated copper and iron salts are removed by treatment with calcium ferrocyanide and filtration. The filtrate is returned to the process. The product obtained by this process meets the U.S.P. standard for purity.

Tartar emetic U.S.P. powdered in drums was quoted in 1954 at 61-62¢ per pound.

### Economic Aspects

The principal producers of tartaric acid and tartrates are the U.S., England, France, Italy, Germany, and Spain. The total annual output of crude tartars expressed as 100% tartaric acid is estimated at 100,000 tons in the Mediterranean countries alone. To this must be added a considerable potential recovery from the U.S. and South America, where the wine production is increasing from year to year, but for various reasons the recovery of tartars has been less efficient than in Europe.

The U.S. does not produce sufficient raw material for its manufacturing capacity of tartaric acid, hence large quantities of lees and argols are imported from the Mediterranean countries and from South America. The tartars are bought on the basis of total tartaric acid content as determined by the Goldenberg analysis (2). Owing to high freight rates, tartars of less than 40% tartaric acid are not shipped overseas. Table IV shows U.S. imports for 1950-52, based on U.S. Tariff Commission figures.

TABLE IV. U.S. Imports of Crude Tartars (Gross) in Lb.

Country	1950	1951	1952
Algeria	3,799,010	3,999,623	3,965,852
Brazil	—	—	33,091
Chile	—	693,943	224,706
France	4,033,046	1,940,900	1,415,964
French Morocco	236,608	445,920	774,368
Italy	3,450,366	3,441,199	41,804
Peru	—	9,810	—
Portugal	1,603,770	3,680,858	330,690
Tunisia	2,836,473	1,049,395	—
<i>Total</i>	15,959,273	15,270,648	6,786,475
Av. price on the basis of 1 lb. tartaric acid contained in crude delivered to N.Y., ¢/lb.	10	16	22

The available tartars far exceed the demand for refined tartaric acid and tartrates. Furthermore, the value of tartars is negligible compared with the value of wines from which they originate. The price picture is determined by the cost of converting a waste product to a salable raw material for refined tartrates as compared with its fertilizer value, determined mainly by the potassium content. Potassium is taken out of the soil of the vineyard and must be replaced in the form of either tartars or other potash fertilizer, whichever form is cheaper.

In view of these facts it is unlikely that a cheaper raw material will become avail-

able in the immediate future, or that the natural product will be replaced by a synthetic tartaric acid.

### Uses

*Tartaric acid* is employed like citric acid in the preparation of carbonated drinks, especially grape-flavored. It is widely used in effervescent tablets and powders, frequently admixed with citric acid. Tartaric acid is an acidulant in the manufacture of gelatin dessert and in fruit jellies, especially in pectin jelly candies when the setting characteristics of the product depend on a relatively low pH. In the manufacture of starch jelly candies, tartaric acid and cream of tartar are used to modify the starch so that the product will flow freely while being cast. It finds use in the cleaning and polishing of metals. In the textile industry it is used in calico printing for controlling the liberation of chlorine from bleach powder. The acid is employed in certain types of photographic work for printing and developing. Some of the iron salts are light-sensitive and hence find application in blue printing (see *Printing and reproducing processes*). The complexing ability of tartaric acid and its alkali salts has been employed to advantage in electroplating (*q.v.*) processes, for instance in the plating of copper from cyanide Rochelle salt baths, and as a sequestering agent (*q.v.*) in aluminum etching (18,20).

*Rochelle salt* is used in the silvering (*q.v.*) of mirrors for which purpose no truly satisfactory substitute exists. Rochelle salt crystals exhibit piezoelectricity and this property makes them valuable, when suitably cut, as components of crystal-controlled electronic oscillators. Rochelle salt finds use in medicine as a mild saline cathartic in preparations like compound effervescing powder (N.F. IX) or Seidlitz powders (see *Cathartics*). In the food field, it is used as an emulsifying agent in the manufacture of processed cheese. In the laboratory it is an ingredient of Fehling's solution for the determination of reducing substances, especially sugars. The use of tartrates in concentration of 0.1–100 p.p.m. has been suggested as an effective method for corrosion and tuberculation inhibition in water systems (23).

*Cream of tartar* finds application in the food field in baking powder (*q.v.*), where its limited solubility in the cold inhibits the reaction with bicarbonate until baking temperature is reached, thus releasing the major portion of the carbon dioxide at the optimum time. The slightly acid, pleasant taste of cream of tartar and its ability to partially invert cane sugar makes the compound useful as an addition to hard candy, taffies, and similar products where partial inversion prevents undesirable crystallization. A slurry of cream of tartar is an excellent cleaner of brass. It is used in the electrolytic tinning of iron and steel, in gold and silver coating of various metals, and in some metal coloring processes.

*Tartar emetic* is used medicinally in small doses as an expectorant in cough sirups, in larger doses as an emetic, and in ampuls for intravenous injection in the treatment of various tropical infections, such as trypanosomiasis and kala-azar. Tartar emetic has found extensive use in agriculture for the control of various kinds of insects. The compound is used as a mordant in fixing basic colors on cotton, leather, and fur. The fastness to washing and light of antimony-tannin-basic dyestuff lakes is used to good advantage in textile printing. Incorporation of tartar emetic in vinyl chloride formulation has been found to inhibit or retard discoloration. See also *Anthelmintics*, Vol. 1, p. 937; *Emetics and expectorants*, Vol. 5, p. 680.

## Bibliography

- (1) Alexander, M., *A New General System for Naming Stereoisomers. I. Report of the Advisory Committee on Configurational Nomenclature* (by H. B. Vickers, Chairman). *II. Proposed Rules for Naming Stereoisomers* (by G. E. McCasland), 1953. (Available from *Chemical Abstracts*, Ohio State University, Columbus 10, Ohio.)
- (2) Allen, A. I., *Commercial Organic Analysis*, 5th ed., Blakiston, N. Y., 1923, Vol. I, p. 724.
- (3) Black, J. W., *Ind. Chemist*, **14**, 443, 483, 521-24 (1938); **15**, 100-1 (1939).
- (4) Black, J. W., *Ind. Chemist*, **15**, 270-76 (1939).
- (5) Buogo, G., *Giorn. chim. ind. appl.*, **16**, 120-22 (1934).
- (6) Church, J. M., and Blumberg, R., *Ind. Eng. Chem.*, **43**, 1780 (1951).
- (7) Ciapetti, G., *Industrie chimique*, **25**, 79 (1938).
- (8) Dale, J. K., and Rice, W. F., Jr., *J. Am. Chem. Soc.*, **55**, 4985 (1933).
- (9) Del Bono, A., *Giorn. chim. ind. appl.*, **15**, 451 (1933).
- (10) Davis, H. D., "Tartaric Acid Processes in Germany," *FIAT Final Rept.*, **1049** (1947).
- (11) Finkle, P., *J. Biol. Chem.*, **100**, 349-55 (1933).
- (12) Legault, R. R., Nimmo, L. L., Hendel, C. E., and Notter, G. K., *Ind. Eng. Chem.*, **41**, 466 (1949).
- (13) Metzner, E. K., *Chem. Eng. Progress*, **43**, 160 (1947).
- (14) Milas, N. A., and Terry, E. M., *J. Am. Chem. Soc.*, **47**, 1415 (1925).
- (15) Overell, B. T., *Australian J. Sci.*, **15**, 28-29 (1952).
- (16) Peerdeman, A. F., von Bommel, A. J., and Bijvoet, J. M., *Proc. Koninkl. Ned. Akad. Wetenschap.*, **B54**, 16-19 (1951); *C.A.* **45**, 5019.
- (17) Phares, E. F., Mosbach, F. H., Denison, F. W., Jr., and Carson, S. F., *Anal. Chem.*, **24**, 660 (1952).
- (18) Prescott, F. J., Shaw, J. K., and Lilker, J., *Metal Finishing*, **51**, 65 (1953).
- (19) Rabaté, J., and Gourévitch, A., *J. pharm. chem.*, [8], **28**, 386-97 (1938).
- (19a) Roux, U., *La Grande Industrie des Acides Organiques*, Dunod, Paris, 1923.
- (20) U.S. Pat. 2,168,909 (Aug. 8, 1939), R. B. Mason (to Aluminum Co. of America).
- (21) U.S. Pat. 2,197,021 (April 16, 1940), R. Pasternack and E. V. Brown (to Chas. Pfizer and Co.).
- (21a) U.S. Pat. 2,359,929 (Oct. 10, 1944), E. K. Metzner (to Stauffer Chemical Co.).
- (22) U.S. Pat. 2,417,230 (March 11, 1947), W. E. Barch (to Standard Brands).
- (23) U.S. Pats. 2,529,177; -178 (Nov. 7, 1950), W. L. Nieland *et al.* (to W. L. and L. D. Betz).
- (24) U.S. Pat. 2,559,650 (July 10, 1951), L. B. Lockwood and G. E. N. Nelson (to U.S. of America).

RICHARD PASTERNAK

**TARTAR REMOVERS.** See *Dentifrices*, Vol. 4, p. 933.

**TAURINE**,  $\text{NH}_2\text{CH}_2\text{CH}_2\text{SO}_3\text{H}$ . See *Bile constituents*, Vol. 2, p. 512.

**TAUROCHOLIC ACID**,  $\text{C}_{26}\text{H}_{46}\text{NO}_7\text{S}$ ; **TAURODESOXYCHOLIC ACID**,  $\text{C}_{26}\text{H}_{45}\text{NO}_6\text{S}$ .  
See *Bile constituents*.

**TAUTOMERISM.** See *Isomerism*, Vol. 8, p. 75.

**TAZETTINE**,  $\text{C}_{18}\text{H}_{21}\text{NO}_5$ . See *Alkaloids*, Vol. 1, p. 494.

**TDE**,  $(p\text{-ClC}_6\text{H}_4)_2\text{CHCHCl}_2$ . See *Insecticides*, Vol. 7, p. 895.

**TEA**

There are three primary kinds of tea: green, black, and oolong. Green tea is prepared without fermentation, black tea with fermentation, and oolong tea is partially fermented. Although any variety of tea can be used in the manufacture of tea, certain varieties are better suited for making one or more of the three kinds. The Japanese leaf is better suited for the manufacture of green tea; and the variety in Formosa is better for oolong tea. In China, green, black, and oolong are made from the same



variety grown in different localities. Leaves from the tea plants grown in the East Indies are especially suited for the making of black tea, although a limited quantity of green tea is made in Ceylon and India. Several varieties have been introduced into India, but the Assamese broad leaf, indigenous to Assam, has proved to be the most successful.

The tea plant, *Thea sinensis* L., which is grown commercially for its leaves, is, in its native state, 15-30 ft. in height, but under cultivation its height is restricted to 2-5 ft. Botanists have universally accepted that the single species of Linnaeus alone is valid; the many other supposed species are now recognized as merely varieties. The leaves vary in length from  $1\frac{1}{2}$  to 10 in. and in width from  $\frac{1}{2}$  to 4 in. Mature leaves are rather thick, smooth, and leathery, borne on a short petiole, and arranged alternately on the stem. The leaves are lanceolate and serrated along nearly the whole margin. The flowers are white and fragrant; they are  $\frac{3}{4}$ - $1\frac{1}{2}$  in. in diameter and have five petals and many stamens.

Apparently only wheat has a wider range of adaptability to conditions than tea, as shown by the countries of production. However, although this species as a whole has such a wide geographical range, not all varieties thrive equally well in any one locality.

Leading tea-growing areas of the world include China, Japan, India, Pakistan, Ceylon, Formosa, Indonesia, Central Africa, and parts of the U.S.S.R. Many attempts have been made to cultivate and manufacture tea in the U.S. (9). These have been unsuccessful, except on an experimental scale, because of the cost of labor.

The world production of tea in 1952, according to the most complete available statistics, exclusive of Indochina, the China mainland, and the U.S.S.R. was approximately 1,288,205,000 lb. (see Table I). Acreage for the same area is estimated at 2,000,000 acres. It is impossible to give an accurate breakdown because many countries that reported production figures failed to include acreage. As far as possible, the export of all tea entering world commerce has been considered in Table I, including exports from the China mainland and Brazil (6).

TABLE I. Production and Export of Tea.  
(Thousand Pounds)

Country	Production		Export	
	1940	1952	1940	1952
India	474,022	621,800	352,636	409,594
Pakistan	—	53,146	—	23,971
Burma	—	—	281	—
Ceylon	265,099	316,842	246,370	314,495
Indonesia	181,045	81,265	159,610	70,268
Indochina	—	—	5,408	430
Malaya	1,574	3,785	663	1,703
China	—	—	76,043	12,000
Formosa	24,303	25,534	19,224	20,553
Japan	128,380	127,559	35,953	20,782
U.S.S.R.	28,330	—	—	—
Central Africa	26,959	37,665	23,850	29,919
Iran	2,250 (estd.)	12,000	—	—
Others	2,482	8,609	1,734	6,847
Total	1,134,444	1,288,205	921,772	910,562

### Cultivation

The tea plant thrives from sea level to elevations of 7,000 ft. All other factors being equal, the higher the elevation at which the tea is produced the better the quality. However, this does not apply so strictly to green tea, as some of the finest Japan green teas are produced near sea level. Tea does best in a warm, wet climate, where most of the rainfall takes place during the plucking season. Also, it grows best in a deep, fertile, well-drained, easily penetrable loam or clay-loam soil containing a substantial amount of well-decomposed organic matter.

The tea plant is generally produced from seed in most tea-producing countries with the exception of Formosa, where propagation generally takes place by branch layering or cuttings.

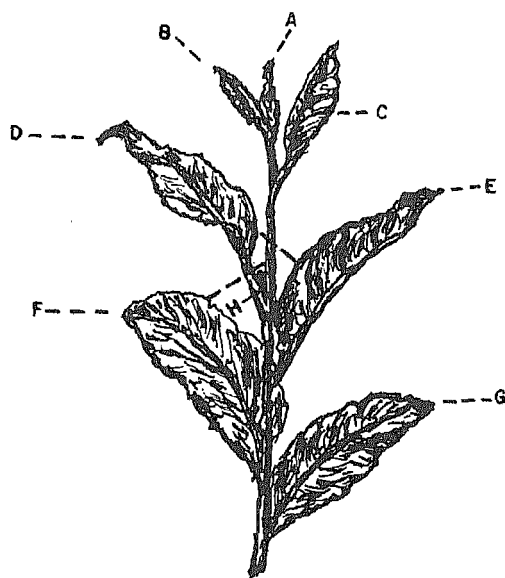


Fig. 1. Tea shoot, showing leaves used for different grades of tea.

The bushes are pruned and kept at a height of 2-5 ft. for convenience in plucking the leaves and to cause the continued growth of new leaves. The tea plant produces a "flush" or full complement of leaves about every 40 days. In China, Formosa, and Japan these flushes are plucked when the majority of the leaves in flush have reached the proper stage of growth, whereby the largest possible amount of the flush can be utilized at one time. These gatherings are known as crops, and they differ in quality. There are a first, second, third, and, sometimes, a fourth crop. They are also referred to as spring, summer, autumn, and winter production. These crops are all of different quality; in China and Japan the first crop produces the best teas, whereas in Formosa the second crop is the best. In Ceylon, India, Java, Sumatra, and other tea-growing countries, the tea planter does not wait for a fully mature flush but picks every 7-15 days; in other words, there are many pluckings during each flush. This results in a larger yield of good, uniform tea, as nearly all the leaves in a flush are gathered at the best time and not so many extremes of quality are produced as in Japan, China, and Formosa, where much hand work has to be done in sorting.

The leaves on a shoot containing a full complement of leaves (see Fig. 1) are known as follows: (A) pekoe tip or flowery pekoe, (B) orange pekoe, (C) pekoe, (D) first souchong, (E) second souchong, (F) first congou, and (G) second congou (9). The second congou is sometimes known as bohea. (H) indicates a leaf bud that will eventually be a full complement of leaves.

In Ceylon, India, Pakistan, Java, Sumatra, and other countries that use this form of leaf grading for black tea, the separation is done by machine, but the separation is only partial and the grading is not followed.

## Processing

### GREEN TEA

In the preparation of green tea, the first step taken after the leaves are plucked is to inhibit the oxidizing enzymes as completely as possible. Various methods are in use. In China the tender young leaves are quickly stirred in pans heated to 250°F., or even higher, over a charcoal fire. This method is also used in Formosa, where much green tea resembling Chinese green tea has been processed in recent years because of the prohibition of the importation of Chinese mainland green teas into the U.S. In Japan the leaves are heated for a short time with live steam, as is also done in India and Ceylon when green tea is made.

In India at present, the green tea is manufactured mostly by machinery and the entire process is accomplished in about 2 hr. in contrast to the average 24 hr. required for black tea. In the manufacture of green tea, every precaution is taken not to bruise the fresh leaves or let them become overheated before manufacture. The steaming of the fresh leaf (200-lb. charge) takes place in a wooden or metal cylindrical drum rotating at about 15 r.p.m. As each charge is completed, it is dumped on the floor and cooled by spraying with cold water and centrifuged. Centrifuging removes 7½ gal. per charge of a yellowish liquid, which contains ½ lb. of solid matter per gallon, of which 2½ oz. is tannin and ½ oz. caffeine. The tea is then repeatedly rolled and heated until dry. When the tea is finally rolled and dried, it is a dark olive-green color. After grading, teas for export to countries where glazing or facing is permitted are faced with 1% French chalk to improve their appearance. Artificially colored or faced teas may not be imported into the U.S., as they do not meet government standards of purity.

### OOLONG TEA

In the curing or manufacture of oolong tea, the process of oxidation by enzyme action is permitted to develop only partially before oxidation is inhibited by heat. In Formosa, where most of the oolong tea is now produced, the tea leaves are stirred and tossed in the sun in large shallow baskets. When the leaves turn brown around the edges and become partially withered, the oxidation enzymes in the leaf are inactivated or destroyed by stirring the leaves in hot pans heated to about 250°F. The leaves are then rolled by hand or machinery, after which they are dried over charcoal fires in hourglass-shaped baskets. However, teas for export are sorted and refired over charcoal fires at a low temperature for 6–8 hr. The better-quality teas are fired at lower temperatures for longer periods. In this treatment, the temperature is judged entirely by the operator, with no thermometer or other measuring device. The quality

teas made by this process in both China and Formosa are very flavory, and the liquor is of varying shades of amber, according to the degree of oxidation before firing.

#### BLACK TEA

There are four important steps in curing black tea: withering, rolling, oxidation or fermentation, and firing or drying. Withering is a preparatory step to rolling; it results in a desired loss of water and a flaccid mechanical condition of the leaf. Rolling determines the strength of a tea and prevents in a measure its deterioration. Oxidizing imparts to black tea its color and flavor. Firing or drying develops the aromatic principle in tea (9).

**Withering.** About 75% of fresh tea leaf consists of water, nearly half of which must be removed so that the leaf will withstand rolling without breaking. The usual method is to expose a thin layer of the leaves to the atmosphere for 18-24 hr. Artificially heated and dried air has been used, as well as withering machines in which the leaves are tumbled in a current of warm air. In many cases the temperature used in this method is too high for best results (ref. 2, pp. 292-306). The natural method, which is the best, depends on high air speeds and low relative humidities. The best withering results during cold weather, when the low humidity counterbalances the low temperature. The best natural witherings take place within 18-24 hr. at 60-80°F. (ref. 4, pp. 130-32).

It is believed that two kinds of changes take place during withering, one physical, when the leaves become flaccid, and one chemical, during which the familiar fruity flavor of fresh apples is developed. In the perfect wither these two conditions occur at the same time (ref. 4, p. 128).

During withering the leaf continues to respire, but the rate of respiration decreases as the withering proceeds. The withering leaves take in oxygen and expel carbon dioxide, and as a result the total solid matter in the leaf may decrease by as much as 5% of the total. It is believed that the tannin content of the leaf does not change during withering; on the other hand, water-soluble nitrogenous compounds in the leaf other than caffeine increase slightly. Although these changes might be regarded as minor, it is probable that a change in the physical state of some of the substances in the cell sap during withering may influence the course of changes taking place later in the manufacture, such as the capacity of the leaf proteins to precipitate certain tannin substances (ref. 5, pp. 84-85).

**No-Wither Systems.** Although withering has been considered indispensable in producing quality teas, systems have been devised to eliminate this step. In one system used in India the freshly picked leaf is put through a chaff cutter or tobacco cutter, rolled, fermented, and fired. The tea from these broken leaves has good body and is especially suited for use in countries such as Canada and the U.S., where tea balls are popular, and in the British Isles and Ireland, where broken teas are popular.

In a similar method the tea was forced through a power food grinder, rolled, fermented, and fired. This process should show an advantage (8). Another development has been the use of the Clivemeare roller, in which the leaves are pulped between steel rollers, then fermented and fired. The product is then made into tablets or cakes. This process is only experimental.

Because of increased labor costs in tea-producing countries and the increased attention being paid to broken teas, no-wither processes should become more important in the future.

**Rolling**, whether accomplished by machinery or hand, causes the cells to burst so that the juices may be liberated and spread over the surface of the leaf. Here these juices come in contact with air, and the oxidizing enzymes begin oxidization of the tannins. Since oxidation (or fermentation) really starts during rolling, these two steps are intimately connected (ref. 5, p. 85). Besides pressing out the juices, which are oxidized and finally dried in and on the leaf to become readily soluble in boiling water, rolling to a great extent governs flavor. Lighter rollings are utilized for high-grown flavory teas or peak season teas. In the production of heavy-bodied teas, however, heavy pressure is utilized to bring out as much juice as possible. Other things being equal, body is always obtained at the expense of flavor, and the opposite is also true. Rolling for strength requires a greater length of time and much more pressure than rolling for flavor does. Under any condition, heating up of the roll should always be avoided. Therefore lifting the pressure cap of a mechanical roller or adjusting of the side battens from time to time to aerate the roll is absolutely necessary. Since the younger and tenderer leaf in a roll is completed first, the roll should be removed and a separation of the fine from the coarse made in the "ball breaker." The fine leaf goes to the fermenting room, and the coarse leaf returns to the roller for completion before oxidation or fermentation. The number of rolling periods and their duration vary at different seasons and in accordance with the purpose. Therefore, a roll or some part of a roll may be going on for 1 to 2 hr. and even longer. Heavy and long rolling is generally practiced on poor-quality teas, since body is the redeeming feature (ref. 4, pp. 162-67). Rolling reduces the surface of the leaf, imparting to it the familiar twist of most commercial teas and thus helping to retain the aroma and reducing the surface exposed to oxidation after firing and grading. This is especially true of leaf teas.

**Oxidation (fermentation)** starts as soon as the rolling begins and the juices of the leaves are exposed to the air and to the oxidizing action of enzymes. The leaves turn red owing to oxidation of the tannin, and at the same time the essential oil of tea is formed. These changes are collectively spoken of as "the fermentation of tea." Nanninga showed that, the longer the fermentation, the greater the percentage of insoluble substances in the leaf; in fact the total solubles fell from 62 to 50%. The best temperature for fermentation is 75-80°F. Humidifiers are used to aid in maintaining the temperature below 84°F. In addition, a high humidity is necessary to keep the fermenting leaf moist. A humidity of 95% is ideal. The common methods of humidification are spraying the walls of the fermenting room and hanging wet cloths in the room. Below 75°F., the oxidation of the tannin is so slow that, by the time it has advanced far enough for the leaves to be of the right copper color, the aroma is lost. If the temperature is too high, the tannin oxidation is too rapid and may be finished before the aroma has had time to develop fully. Much work has been done on the oxidizing enzyme of tea, which was discovered almost simultaneously by Bamber in Ceylon and Nanninga in Java. In Japan, Azo also showed that the oxidation was assisted by an enzyme. He concluded that the steaming step in green tea manufacture inactivated this enzyme and was the cause of the chief difference between green and black tea.

The oxidizing enzyme in tea produces a reaction that does not take place in the living cell. These enzymes are inactivated above 140°F. This oxidizing enzyme has been separated from the tea leaf; yeast has also been isolated, but the yeast does not seem to play a major role in tea fermentation. However, some observers think that yeast may be responsible for the production of seasonal and district flavors other than

the flavors caused by the essential oil of tea. Fresh leaf also contains bacterial flora which apparently play no part in fermentation (ref. 5, pp. 85-88).

During fermentation the leaf changes from a dark green to a bright coppery color, and the leafy odor or "nose" is converted into a characteristic fruity one. Strict attention must be paid to these characteristics, and the moment they are reached the tea should be fired or dried.

**Firing or Drying.** During this step in the manufacture of black tea oxidation ceases, and the leaf enzymes are inactivated. The water-soluble tannins show a slight decrease, and some tea aroma is lost. During firing the moisture is reduced from about 65%, more or less according to the wither, to about 2%. The moisture content, however, rises rapidly during sorting.

In firing tea successfully in the conventional dryers (used in India, Ceylon, Java, and where machine drying is in use), manufacturers differ as to the maximum safe temperature. From 190 to 200°F. is often used, but some gardens fire at even lower temperatures. The water-soluble tannin in the leaf shows only a slight decrease during firing, and there is no important change in the other constituents of the leaf.

Some slight change takes place after tea is fired, and small quantities of carbon dioxide are given off. On keeping, tea goes through a mellowing process which includes a loss of bitterness and rawness. This is caused by a further slight oxidation of the tannin without the aid of the leaf enzyme (ref. 5, p. 131). Tea is best packed for shipment with a moisture content of about 6% (ref. 5, p. 296).

In preparing China black tea the steps in the process not only differ from the curing of black tea in India, Ceylon, Java, Sumatra, and Africa, where the cold-fermentation process is used, but they also show a number of variations and modifications in different localities and even in the same locality. China black teas are oxidized in the sun or are otherwise warmed during oxidation. Thus they are known as "warm-fermented" teas.

In China, flavor is the chief consideration in the curing of black tea. The method of preparation tends to decrease soluble tannin, and the teas are much milder, partially because the rolling is very thorough and the oxidized tannin formed in the process is largely precipitated by the leaf proteins. In the East Indian type of cold fermentation, the purpose is to produce thick, strong, pungent liquors, and to accomplish this it is necessary to keep as much tannin and tannin products in the soluble state as possible (ref. 5, p. 133).

### Chemistry of Tea

Fresh tea leaves contain about 25% solid matter. The frame of the leaf is made up of cellulose and fiber which, with pure proteins, comprise most of the water-insoluble matter. The water-soluble constituents of the leaf are tea tannin, caffeine, protein bodies, gummy matter, and sugars. The leaf also includes small quantities of mineral matter, chlorophyll pigments, flavones, anthocyanins, waxes and resins, mucilages and pectic bodies, oxalic acid, gallic acid, and compounds of the purine group other than caffeine. Black tea, in addition to the above substances, contains oxidized tannin products and essential oil of tea. Green tea is entirely devoid of these two substances (ref. 5, pp. 88-89). Chlorophyll and its allied pigments, the flavones and anthocyanins, which are chemically closely related, occur in small quantities in Japanese green tea. However, the amount of these two constituents is very important. Fla-

flavones are yellow substances that give color to a green tea infusion but are tasteless. Anthocyanins are bitter and are detrimental to quality.

A simple test has been developed for the rapid estimation of anthocyanins in a green tea infusion. A few drops of dilute hydrochloric acid is added to a tea infusion. If anthocyanins are present, a red coloration occurs which is measured against a scale of standard colors. The more anthocyanins, the poorer is the quality of the tea. It has also been found that the desirable flavones vary inversely to the anthocyanins in the leaf.

The famous Gyo Kuro teas, grown under shade, have less tannin than the Sencha teas, which are grown in the sun. The shaded tea also contains a larger amount of caffeine and does not contain anthocyanins.

The *caffeine* (*q.v.*) content of tea averages about 3%. Several other members of the purine group besides caffeine have been reported in tea; they include xanthine, hypoxanthine, adenine, theobromine, and theophyllin, which has been isolated from tea in minute quantities. (See Vol. 1, p. 474.)

The *essential oil of tea*, which supplies the aroma and much of the flavor, occurs only in black tea and is formed during fermentation. This essential oil does not occur in fresh or withered leaf but results from the action of oxidizing enzymes on the leaf juices during and after rolling. The essential oil is prepared by distilling black tea with steam and extracting the oil from the distillate. The essential oil of tea occurs in such minute quantities that it is difficult to study (ref. 10, Vol. I, p. 523).

No reference to essential oil of tea being present in oolong (semifermented) teas has been found. However, since the tannins in oolong teas are partially oxidized before enzyme action is inhibited by sterilizing and firing, it is very probable that oolong teas contain some essential oil.

Green teas have flavor and aroma, but, since the juices of these teas are not oxidized or fermented by enzyme action, the aroma is not due to what is known as tea essential oil but is believed to be due to the natural flavor or "spirit" of tea that exists in the fresh leaves before manufacture (ref. 5, pp. 127-28). If this is correct, the manufacture or curing must do much to develop or change this natural flavor in green teas. These flavors are not so volatile and are more lasting than those of the black teas, in which the flavor is attributed to the essential oil.

*Tea tannins* are entirely different from the tannins found in the bark of certain plants and employed in the tanning industry. See *Tanning materials*.

Tea tannin, although it does combine with proteins in tea, will not tan skins. It belongs to the pyrocatechol group of tannins. During rolling and fermentation in making black tea, tannins are acted on by oxidizing enzymes in the leaf to form substances varying in color from light red to brown and soluble to varying degrees in water (ref. 2, p. 431).

Pure tea tannin is a white powder which easily oxidizes in the air to a brown gummy mass. In the presence of moisture this change is very rapid. Tea tannin is easily soluble in water, ethyl alcohol, methanol, acetone, and acetic anhydride; it is less soluble in sulfuric and acetic acids; it is insoluble in chloroform, benzene, and dry ether (ref. 10, Vol. I, p. 316).

Tea tannin differs from those tannins used in tanning in several ways. It does not form the same type of precipitate with gelatin as ordinary tannins. The precipitate with tea tannin is decomposed by dilution and forms only in a concentrated solution. On oxidation, however, the tea tannin forms an insoluble precipitate similar

to that of ordinary tannin. Tea tannin has a bitter taste, rather than the astringent taste of other tannins. With alkaloids, both tea tannin and ordinary tannin produce a precipitate, but the precipitate with tea tannin is easily decomposed by water. In acid solution it forms an insoluble red precipitate of "tannin red" ("phlobaphenes"), as do the pyrocatechol tannins. Like ordinary tannin, tea tannin produces a blue color with ferric chloride solution. Unlike ordinary tannin, tea tannin did not cause constipation when large doses (45 grains per day) were administered for three consecutive days (3,5). This is equivalent to about 18 cups of strong tea per day.

For the determination of tannin and other constituents of tea see reference (1). An analysis of Assam tea (cold-fermented-type black tea) is shown in Table II. Since the amount of oxidized tannin products is the same for 5-min. and 1-hr. extraction, these substances must be mainly located on the outside of the leaf where they are easily extracted (ref. 5, pp. 90-91).

TABLE II. Analysis of Assam Tea.

Substance	Total water-soluble, %, boiling 1 hr.	Total water-soluble matter, % 5-min. infusion
Tea tannin	12	7
Caffeine	4	3
Protein bodies	12	6
Gummy matter	2	1
Sugars	1.5	1
Soluble minerals	4	2.5
Oxidized tannin products	2	2
<i>Total soluble solids</i>	<i>37.5</i>	<i>23.0</i>

Source: Ref. (5).

In soft, succulent young leaf plucked in Assam not only the tannin but also the caffeine and water-soluble solids were higher than in poor leaf, which was harder and drier, having been plucked in an unfavorable part of the season, but still young.

**Teaseed Oil.** Teaseed oil (see Vol. 6, pp. 144, 147) must not be confused with the essential oil of the fermented tea leaf that helps to give black tea its flavor. Tea bushes for the production of commercial tea produce little or no seed, because of pruning, but, where plants are allowed to grow to produce seed for planting in establishing new gardens, large quantities of seed are produced. Practically all teaseed oil is produced commercially in China, Indochina, and Japan. Deuss found an average of 42% oil in tea seed produced in Java. The seed from China bushes contained 30-35%, and that from Assam bushes 43-45%.

The color of the oil ranges from yellow to orange, and it is a nondrying oil. The crude oil has an unpleasant odor and is very bitter to the taste. Both the bitter taste and the odor can be removed by refining. The finest quality oil is used for dressing the hair, and the better grades of the ordinary oil are used for edible purposes, chiefly in the localities where produced. The poorer grades are used in soap manufacture and as an illuminant (ref. 10, Vol. I, p. 526).

### Grading

All teas are graded, some for quality grades (cup tests), some for style or leaf grades, and some for both. The most important gradings of the most important teas, especially those sold in the U.S., are given below.



**China Green Tea.** Everything else being equal, the higher the altitude at which the tea is grown, the better is the quality. Moyune and Teenkai districts produce the finest quality; medium-quality teas are produced in Hoochow; and the low-quality teas are produced in the Ping Suey District. The leaf or style grades, determined by passing the finished tea through sieves, give such grades as Young Hyson, Hyson, Pinhead Gunpowder, Gunpowders, Imperials, and Pea Leaf; these grades are further subdivided into many styles, generally by using numbers such as Gunpowder No. 1, 2, and 3.

**Japanese Teas.** In Japan, district names determine quality, such as Yamashiro and Enshu. Japanese teas are made principally into pan-fired, basket-fired, and natural leaf. Other kinds such as Gyokuros, ceremonial teas, and Bancha are mainly for home consumption.

**Oolong.** Oolong teas are by far the most flavory and come from both Formosa and the China mainland. The principal oolongs from China are known as Foochow, Axmoy, and Canton. However, in recent years they have to a large extent been superseded by Formosa oolongs. Oolongs are often scented with flowers such as gardenia, rose, and jasmine.

**Black Teas.** The black teas of China, which are known as the warm-fermented teas, have no definite leaf grades. The most important of the China black teas are the North China or black leaf congous, the finest of which are Keemuns, Ningchows, and Ichangs; the South China or red leaf congous, the most important of which are Packhums, Packlings, and Panyongs. The well-known Lapsang souchong, a large leaf congou generally with a smoky flavor, is highly prized in both Great Britain and America among connoisseurs. At this time (1954) there is a prohibition, declared by the Foreign Assets Control, against China teas entering the U.S.

**East Indian Type Tea.** East Indian type (cold-fermented) black teas, like those from India, Ceylon, Java, Sumatra, Africa, and other countries where this type is made, constitute more than 95% of the teas now consumed in America.

The simplest form of grading include the leaf grades of orange pekoe (O.P.), pekoe (P), pekoe souchong (P.S.), and souchong (S), and the broken grades fannings (F), broken orange pekoe (BOP), broken pekoe (BP), broken pekoe souchong (BPS), and broken souchong (BS). Most of these separations are accomplished by using a series of oscillating sieves or revolving cylindrical sieves. However, this grading is only for style classification, and the market value of the tea has to be judged and evaluated by the tea taster.

### Legislative Aspects

The quality of teas imported into and distributed in the U.S. is largely controlled under the Tea Act of 1897, as amended. The original Tea Act passed in 1883 was one of the first U.S. laws controlling the quality of food products. Under this law, all tea imported into the U.S. is examined by standard methods, such as those used in the tea trade, to determine whether they meet certain minimum standards. Those failing to meet these standards are rejected. Early types of adulteration included foreign coloring matter, exhausted leaves, leaves of other plants, and glazing materials. Most of this adulteration has disappeared under the administration of the Tea Act (7).

## Bibliography

- (1) A.O.A.C., *Methods of Analysis*, 6th ed., Washington, D.C., 1945, pp. 219-22.
- (2) Ball, C., *India Tea, Its Culture and Manufacture*, 5th ed., W. Thacker and Co., London, 1940.
- (3) Carpenter, P. H., and Harler, C. R., *Tea. Assoc. Quart. J., Calcutta*, **1932**, pt. 1.
- (4) Elliot, E. C., and Whitehead, F. J., *Tea Planting in Ceylon*, The Times of Ceylon Co., Colombia, Ceylon, 1926.
- (5) Harler, C. R., *The Culture and Marketing of Tea*, Oxford Univ. Press, London, 1933. Table II courtesy Oxford University Press.
- (6) International Tea Committee, London, 1952-53, *Bulletin of Statistics and Supplement*, June 1953.
- (7) Mitchell, G. F., *Tea Coffee Trade J.*, **81**, No. 5, 50 (1941).
- (8) Mitchell, G. F., *Tea Coffee Trade J.*, **107**, No. 3, 56,90,91 (1954).
- (9) Mitchell, G. F., "Cultivation and Manufacture of Tea in the U.S.," *U.S. Dept. Agr., Bur. Plant Industry Bull.*, **234** (1912).
- (10) Ukers, W. H., *All about Tea*, The Tea and Coffee Trade Journal, N.Y., 1935, Vols. I and II.
- (11) Ukers, W. H., and Prescott, S. C., "Coffee and Tea," in Jacobs (ed.), *The Chemistry of Food and Food Products*, 2nd ed., Interscience, N.Y.-London, 1951, Vol. II, ch. XXXI.

(GEORGE F. MITCHELL)

**TEASEED OIL.** See *Fats and fatty oils*, Vol. **6**, pp. 144, 147.

**TECHNETIUM, Tc.** See "Element 43" under *Elements*, Vol. **5**, p. 673; *Nucleonics*, Vol. **9**, p. 534.

**TECTOSILICATES.** See *Silica and silicates (mineral)*, Vol. **12**, pp. 276, 292.

**TELEVISION.** See *Electronics*, Vol. **5**, p. 601.

## TELLURIUM AND TELLURIUM COMPOUNDS

Tellurium, Te, atomic number 52, atomic weight 127.61, is in Group VI of the periodic table, below sulfur and selenium, and between antimony and iodine horizontally. It was discovered by Müller in 1782 and named by Klaproth sixteen years later from the Latin *tellus*, earth. The tellurium atom has the electronic configuration 2-8-18-18-6 where the six outer electrons are  $5s^2 5p^4$ . The stable tellurium isotopes have mass numbers 120, 122, 123, 124, 125, 126, 128, and 130. Tellurium is more metallic than oxygen, sulfur, or selenium, but still resembles them closely in most of its chemical properties.

The amount of tellurium in the earth's crust is estimated to be 0.002 p.p.m., considerably less than that of selenium (16). Tellurium is used almost entirely in the rubber industry as a secondary vulcanizing agent and in metallurgy to modify and improve the properties of cast iron, lead, and copper alloys. It sells at about \$2.10 per pound. There has also been considerable recent interest in the chemistry of tellurium, as it is one of the more plentiful fission products of uranium.

**Physical Properties.** Elementary tellurium does not show as many allotropic forms as sulfur and selenium. Only a hexagonal crystalline form, isomorphous with hexagonal (gray) selenium, and an amorphous form of uncertain properties have been reported. The element is silvery white in appearance and has a definite metallic glance. It is brittle but not hard. The density of tellurium is near 6.2 g./cu.cm. Solid tellurium is a poor electrical conductor and light has only a slight effect on its conductance. Thin films of tellurium are opaque to visible light but are useful as infrared transmitting films.

The entropy of solid tellurium is 11.88 e.u. at 25°C. Tellurium melts at 450°C. to give a dark liquid resembling molten lead. The heat of fusion is 4,180 kg.-cal./mole  $\pm$  130 cal. The vapor pressure between 786 and 1110°K. is given by the equation (3):

$$\log p_{\text{mm}} = 7.5999 - (5960.2/T)$$

where  $T = ^\circ\text{K}$ . The extrapolated boiling point is 990°C. The specific heat is 6.14 cal./g. at 25°C. Tellurium vapor absorbs light in the visible and ultraviolet regions and, according to mass spectrographic studies, contains some  $\text{Te}_5$ ,  $\text{Te}_4$ ,  $\text{Te}_3$ , and  $\text{Te}_2$  molecules as well as Te atoms. The heat of formation from the standard state of a Te(g.) atom is 48 kg.-cal./mole. Electron diffraction and vapor density studies indicate that  $\text{Te}_2$  is the most abundant vapor species from 600 to 2100°C. The dissociation energy of  $\text{Te}_2(\text{g.})$  to form atoms is 53 kg.-cal./mole.

The covalent radius of a tellurium atom is 1.37 Å. The first electron affinity may be as high as 2.3 e.v. while the second electron affinity (to form  $\text{Te}^{2-}$ ) is about -3 e.v. The first ionization potential is 9.01 e.v., and the electronegativity is about 2.2 on the Pauling scale. Extensive data and references are given by Gmelin (9).

**Chemical Properties.** Chemically, tellurium generally resembles sulfur and selenium. It forms ionic compounds containing the  $\text{Te}^{2-}$  ion when reacted with active metals, and covalent compounds with other elements. Solid crystalline tellurium tarnishes only slightly in air; molten tellurium is readily oxidized to tellurium dioxide. Tellurium reacts with halogens, and mixes in all proportions with sulfur and selenium. Oxidation of tellurium with concentrated nitric acid and igniting the  $2\text{TeO}_2 \cdot \text{HNO}_3$  yields very pure  $\text{TeO}_2$ . Tellurium reacts with sulfuric acid to form  $\text{TeSO}_3$  and, when tellurium is added to solutions containing the telluride ion, colored polytellurides are formed. Unlike selenium, tellurium is not soluble in aqueous sodium sulfite. This offers a method for separating the two elements. Tellurium is soluble in hot caustic alkalis, but not in ammonium hydroxide. In solution, tellurium forms monatomic anions ( $\text{Te}^{2-}$ ) and cations ( $\text{Te}^{4+}$ ), and tellurium films can be deposited on inert electrodes of either sign.

Organic compounds containing tellurium are not as stable as the corresponding sulfur and selenium compounds, but alkyl and aryl tellurides, telluromercaptans, telluronium compounds, and cyclic tellurium compounds are known.

#### OCCURRENCE (15)

Tellurium, together with sulfur and selenium, is a primary component of intrusive and extrusive magmas, of volcanic gases, and hence, of volcanic sulfur deposits. It is commonly associated with sulfides and selenides, forming the corresponding and often isomorphous tellurides of iron, copper, lead, bismuth, silver, and other metals. In oxidized ores, tellurium is often found as tellurite,  $\text{TeO}_2$ . Native tellurium is also well known.

Tellurium is one of the few elements that combine with gold. Tellurium, gold, and silver are associated in many gold deposits, as  $(\text{Au}, \text{Ag})\text{Te}_2$ ,  $\text{AuTe}_2$ ,  $\text{Ag}_2\text{Te}$ , etc. When present in excessive amounts, tellurium interferes with amalgamating, chlorinating, and cyaniding, and hence reduces gold recovery. Such high-tellurium gold ores are either roasted to drive off the tellurium or smelted with copper or lead ores, which act as a flux. Complete removal of tellurium is essential in gold production, since gold containing over 0.01% Te is too brittle to be rolled. Annealing such gold at low red or black heat only increases its brittleness (19).

Commercial tellurium originates in copper and lead ores. On smelting, it follows the precious metals into the blister copper and crude lead, and on electrolytic refining appears in anode slime.

#### METALLURGY (21)

Tellurium is recovered from electrolytic copper refinery slimes, in which it may be present from a trace up to 4% (21). The slimes are first treated by one of several methods: (1) refining treated slimes with soda ash in doré or cupelling furnace (1,7, 24), (2) a combined oxidation and alkalization by roasting or baking a slimes-soda-ash mix, or (3) boiling the slimes with caustic soda after an oxidizing or a sulfating roast (10,20). (See also *Selenium*.)

The soda slag from (1) or the roasted product of (2) is leached with water to extract sodium tellurite. The liquor from (3) contains lead, probably as sodium plumbite. In all three cases, the solution contains selenium. Whatever the method, the liquor is neutralized to pH 6-6.2 with sulfuric acid to precipitate impure tellurous acid as tellurium mud (37). In addition to tellurous acid, the mud contains lead sulfate, silica, and other impurities. The mud is purified by redissolving in caustic soda and reprecipitating. Impurities such as lead may be removed by precipitating carefully from the caustic solution with sodium sulfide.

Three methods are used to recover elemental tellurium from the mud: (1) direct reduction by heating with flour under a cover of borax; heavy fuming of tellurium dioxide is a drawback; (2) dissolving the mud in hydrochloric acid or in sulfuric acid to which crude common salt is added, followed by reduction with sulfur dioxide, filtration, washing, drying, and melting (31); (3) dissolving in caustic soda and electrolyzing the solution with stainless steel electrodes followed by washing, drying, and melting of the cathode deposit (34)—this is the most satisfactory method.

#### ANALYSIS (22)

The most commonly used procedure is to dissolve the sample in aqua regia and to fume off selenium with sulfuric acid and potassium bisulfate. More sulfuric acid is then added and fumed off. The residue is leached with 10 ml. sulfuric acid and water and the solution, containing tellurium as tellurite, is titrated with potassium permanganate. The reagent must be standardized with telluric acid, as the reaction is not quite stoichiometric. Other volumetric as well as polarographic and potentiometric methods are also employed. When tellurium content is very low, it is estimated spectrographically or determined colorimetrically after precipitating with sulfur dioxide. Duval and Doan (4) have reviewed gravimetric methods for the determination of tellurium.

#### HEALTH AND SAFETY FACTORS (5,11)

Elemental tellurium is not considered to be a health hazard or a cause for serious illness. This applies also to the stable metallic tellurides, that is, those of silver, copper, lead, etc. Nevertheless, tellurium and especially its compounds should be handled with care. Hydrogen telluride is very toxic, and tellurites are said to be more toxic than selenites and arsenites. Tellurium compounds are absorbed into the body through the skin and by ingestion and inhalation of dust, fumes, and vapors. The toxic effects arise on the reduction of tellurium compounds to the relatively harmless elemental tellurium and to methyl telluride. The latter is excreted in exhaled breath,

sweat, urine, and feces. It is characterized by an offensive odor of garlic. No definite pathological effects are observed. Moderate exposure to tellurium dioxide fumes and dust for several weeks causes dryness and metallic taste in the mouth and obnoxious garlic odor of breath, sweat, and urine. These are much more pronounced on exposure to hydrogen telluride.

As with selenium, industrial precautions include the common sense measures of good housekeeping, adequate ventilation, personal cleanliness, and frequent change of clothing. Gloves, dust masks, and chemical goggles should be used where needed. Prolonged or repeated contact of skin with tellurium solutions or compounds should be avoided. Oral administration of ascorbic acid and of chlorophyllin preparations has been recommended to alleviate the unpleasant breath. Chlorophyllin has proved to be the more effective.

Although tellurium and tellurium products present no fire hazard, they should be stored in a cool, ventilated area away from powerful oxidizing agents or areas of acute fire hazard. There are no shipping restrictions.

### Inorganic Compounds

Tellurium forms both inorganic and organic compounds which for the most part are very similar to the corresponding sulfur and selenium compounds. Tellurium shows oxidation states of  $-2$ ,  $0$ ,  $+2$ ,  $+4$ , and  $+6$ .

The most important inorganic tellurium compounds are the tellurides, and the halides, oxides, and oxyacids of tellurium. Detailed descriptions of tellurium compounds are given by Friend (6a), Mellor (17), Yost and Russell (25), and Sidgwick (23). Laboratory techniques for preparation of many tellurium compounds have been described (2,13). Physical properties of some important inorganic tellurium compounds are given in Table I.

TABLE I. Physical Properties of Some Inorganic Tellurium Compounds.

Compound	M.p., °C.	B.p., °C. <sup>a</sup>	Heat of formation (25°C.), kg.-cal./mole
H <sub>2</sub> Te	-57	0	36.9
CS <sub>2</sub> Te	-54	~110	
TeCl <sub>2</sub>	208	328	
TeBr <sub>2</sub>	280	339	
TeF <sub>4</sub>	—	> 97	
TeCl <sub>4</sub>	224	392	-77.2
TeBr <sub>4</sub>	380	(547)	-49.8
TeI <sub>4</sub>	259	(d)	
Te <sub>2</sub> F <sub>10</sub>	-14	60	
TeF <sub>6</sub>	-38	-39(s)	-315
TeO <sub>2</sub>	733	1245	-77.69
H <sub>2</sub> TeO <sub>3</sub>	—	—	-144.7

<sup>a</sup> At the boiling point, the partial pressure of the species indicated is 1 atm.; (s) indicates sublimation; (d) indicates decomposition; and estimated values are enclosed in parentheses.

### Tellurides.

Most metals react with tellurium to form metal tellurides. Polytellurides result when excess tellurium is added to alkali telluride solutions. The alkali and alkaline earth tellurides are ionic solids and are fairly stable. In solution, they are hydrolyzed

less than sulfides or selenides, but are very easily oxidized. The heats of formation of sodium and magnesium tellurides are  $-84.0$  and  $-50$  kg.-cal./mole, respectively. Hydrotellurides, such as  $\text{NaHTe}$ , are also known.

$\text{CSTe}$  is a yellow-red substance with a garlic smell, and is decomposed by light at ordinary temperatures to form carbon disulfide, carbon, and tellurium.

Tellurides of alkali and alkaline earth metals, aluminum, iron, and some other metals form **hydrogen telluride** when attacked by mineral acids. Hydrogen telluride is conveniently prepared by the action of water on aluminum telluride. Hydrogen telluride is colorless in the solid state and pale yellow as a liquid. The gas consists of monomeric  $\text{H}_2\text{Te}$ , has an offensive smell, and is very poisonous. Hydrogen telluride is thermodynamically unstable and cannot be formed by direct combination of the elements. It decomposes slowly on standing. It is possible to produce hydrogen telluride by electrolysis of a 50% solution of sulfuric or phosphoric acid with a tellurium cathode.

### **Tellurium Halides.**

Tellurium halides are formed by action of halogens or interhalogen compounds on elementary tellurium. The action of cobaltic fluoride on tellurium, or of hydrogen fluoride on tellurium oxides gives  $\text{TeF}_2$  and  $\text{TeF}_4$ , but their properties are not well known. No monohalide,  $\text{Te}_2\text{X}_2$ , is believed to exist. Neither does tellurium form well-defined oxyhalides as do sulfur and selenium.  $\text{TeCl}_2$  and  $\text{TeBr}_2$  can be formed by reaction of tellurium with chlorine or bromine, or by reduction of the tellurium tetrahalide with tellurium. They are stable solids which melt and vaporize without decomposition. Tellurium dichloride has a high electrical conductivity and is soluble in ether. Both of these dihalides are hydrolyzed in water to form tellurous acid, tellurium, and the appropriate hydrogen halide.  $\text{TeI}_2$  has also been prepared.

$\text{TeCl}_4$ ,  $\text{TeBr}_4$ , and  $\text{TeI}_4$  are known and may be prepared by reaction of the elements. Tellurium tetrachloride can also be prepared by the action of sulfur monochloride or arsenic trichloride on tellurium. Vaporization of the tetrahalides gives  $\text{TeX}_4$ ,  $\text{TeX}_2$ , and  $\text{X}_2$  molecules in the gas phase. Tellurium tetrachloride is soluble in benzene, toluene, ethyl and methyl alcohols, and hot water. In cold water, tellurium tetrachloride hydrolyzes, forming a precipitate of  $\text{TeO}_2$ . Fused tellurium tetrachloride is a good conductor and therefore must be ionized in the liquid state, although the nature of the ions is unknown. Tellurium tetrabromide forms a clear solution in water. Tellurium tetraiodide (solid) dissociates on heating to give  $\text{TeI}_2(\text{g})$  and  $\text{I}_2(\text{g})$ .

Direct action of fluorine on tellurium yields mainly  $\text{TeF}_6$  with small amounts of  $\text{Te}_2\text{F}_{10}$ . These fluorides are very stable and hydrolyze slowly. Tellurium hexafluoride reacts with mercury at room temperature to give mercurous fluoride and tellurium.

### **Tellurium Oxides and Acids.**

Three oxides of tellurium have been reported:  $\text{TeO}$ ,  $\text{TeO}_2$ , and  $\text{TeO}_3$ . A black solid, prepared by treating tellurium with sulfuric acid to form  $\text{TeSO}_3$  and then decomposing the  $\text{TeSO}_3$ , has the composition  $\text{TeO}$ . Recent work (8) indicates, however, no stable  $\text{TeO}$  solid phase.

**Tellurium dioxide** is the most common oxide and is formed by oxidation of tellurium in air or oxygen, or by oxidation with nitric acid. It is a white crystalline

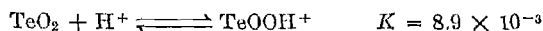
solid which exists in several modifications. The melting point is 733°C., and it forms a dark yellow liquid. The density of the solid is 5.67 g./cm.<sup>3</sup> Tellurium dioxide vaporizes mainly as TeO<sub>2</sub>(g) in the range 790–940°C., and the vapor pressure is given by the equation:

$$\log p_{\text{atm}} = 8.075 - 12,258/T$$

The heat of vaporization over this temperature range is 56.1 kg.-cal./mole. Tellurium dioxide vapor dissociates at higher temperatures to TeO(g) and oxygen.

Tellurium dioxide is only slightly soluble in water (7 mg./liter), forming a dilute solution of tellurous acid.

In alkali hydroxide solutions tellurium dioxide forms alkali tellurites. With strong acids, tellurium dioxide forms addition compounds (2TeO<sub>2</sub>.SO<sub>3</sub>, 2TeO<sub>2</sub>.HNO<sub>3</sub>, 2TeO<sub>2</sub>.HClO<sub>4</sub>, etc.) and the following equilibrium is observed (14):



As an oxidizing agent, tellurium dioxide is similar to selenium dioxide but is less effective and requires higher temperatures.

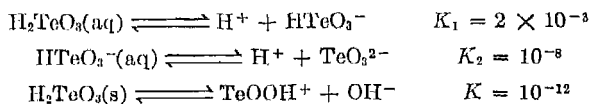
**Tellurium trioxide** is an orange-yellow solid prepared by dehydrating H<sub>6</sub>TeO<sub>6</sub> at 300–360°C. This oxide is not attacked by cold water, cold hydrochloric acid, hot nitric acid, or moderately concentrated potassium hydroxide. Tellurium trioxide oxidizes hot concentrated hydrochloric acid to form chlorine, tellurium dioxide, tellurium tetrachloride, and water. With hot concentrated alkalis, tellurium trioxide forms tellurates. When heated, tellurium trioxide decomposes to form tellurium dioxide and oxygen.

#### ACIDS AND SALTS

The known oxyacids of tellurium contain Te in the +4 or +6 oxidation state. Tellurous acid (H<sub>2</sub>TeO<sub>3</sub>), allotelluric acid (H<sub>2</sub>TeO<sub>4</sub>)<sub>n</sub>, orthotelluric acid (H<sub>6</sub>TeO<sub>6</sub>), and polytelluric acid (H<sub>x</sub>Te<sub>y</sub>O<sub>z</sub>), or their salts are all known. In the higher oxidation state, tellurium shows marked differences from selenium and sulfur.

Solid tellurous acid has apparently not been prepared and tellurium dioxide precipitates from solutions at slightly elevated temperatures. Alkali tellurites are obtained by dissolving tellurium dioxide in strong alkali solutions. In alkaline solutions, tellurites are easily oxidized to tellurates, while in acid solutions, tellurites are easily reduced to tellurium.

Tellurous acid ionizes according to these equations (14):



In acid solutions of tellurium dioxide, TeOOH<sup>+</sup> is reduced to metallic tellurium by sulfurous acid or stannous ion. Halogens and Fe<sup>3+</sup> will oxidize tellurium to TeOOH<sup>+</sup> in the presence of strong acids.

**Telluric acid** has a strong tendency to polymerize, and orthotelluric acid, H<sub>6</sub>TeO<sub>6</sub>, is the common form observed. This compound is formed by refluxing tellurium or tellurium dioxide with hydrogen peroxide and concentrated sulfuric acid, by oxidizing hot nitric acid solutions of tellurium dioxide with chromium trioxide, CrO<sub>3</sub>, or by treating a hot hydrochloric acid solution of tetravalent tellurium with chloric acid or

perchloric acid. Orthotelluric acid exists in two crystalline forms and as a tetrahydrate and when strongly heated loses water to give first *allotelluric acid*,  $(\text{H}_2\text{TeO}_4)_n$ , then tellurium trioxide, and finally tellurium dioxide and oxygen. Orthotelluric acid is soluble in water (30 g./100 g.  $\text{H}_2\text{O}$  at  $18^\circ\text{C}$ .) and forms weakly acidic solutions. The first ionization constant ( $k_1$ ) is between  $10^{-6}$  and  $10^{-9}$ , and  $k_2 \approx 10^{-11}$  (14). Salts in which one or two hydrogens are replaced are well known ( $\text{MH}_5\text{TeO}_6$  or  $\text{M}_2\text{H}_4\text{TeO}_6$ ). Although the acid is primarily dibasic, compounds like  $\text{Ag}_6\text{TeO}_6$  and  $\text{Te}(\text{OCH}_3)_6$  are also known. Since orthotelluric acid is a weak acid, most tellurates can be taken into solution by strong acids.

Telluric acid is a good oxidizing agent and will liberate chlorine from a concentrated hydrochloric acid solution. Hydrogen sulfide reduces orthotelluric acid slowly to tellurium sulfide and disulfide. Tellurium and selenium reduce orthotelluric acid to tellurium dioxide, and sulfur reduces it to tellurium. Telluric acid solutions attack silver, mercury, lead, bismuth, copper, zinc, arsenic, antimony, tin, aluminum, cadmium, and nickel.

Only a few metatellurates, such as  $\text{K}_2\text{TeO}_4$ , isomorphous with the corresponding selenates and sulfates, are known.

### Organic Compounds

Organic tellurium compounds include the telluromercaptans ( $\text{RTeH}$ ), the tellurides ( $\text{R}_2\text{Te}$  and  $\text{R}_2\text{Te}_2$ ), the telluronium halides ( $\text{R}_3\text{TeX}$ ), the mono-, di-, and trihalides ( $\text{RTeX}$ ,  $\text{R}_2\text{TeX}_2$ , and  $\text{RTeX}_3$ ), the telluroxides ( $\text{R}_2\text{TeO}$ ), the telluronones ( $\text{R}_2\text{TeO}_2$ ), the tellurinic acids ( $\text{RTeOOH}$ ), and the telluroketones ( $\text{R}_2\text{C'Te}$ ). Cyclic tellurides are also known.

Similarities with sulfur and selenium compounds are marked except that, in general, organic tellurium compounds are less stable. General preparative methods are useful here. Sidgwick (23) gives useful references to much original work, and details of laboratory preparations for many common organic tellurium compounds are given in *Organic Syntheses* (18), Houben-Weyl (12), and Friend (6b). Melting or boiling points of the more common organic tellurium compounds are given in Table II.

TABLE II. Boiling and Melting Points of Some Organic Tellurium Compounds.

Compound	B.p., $^\circ\text{C}$ .	Compound	M.p., $^\circ\text{C}$ .
$\text{CH}_3\text{TeH}$	57	$(\text{C}_2\text{H}_5)_3\text{TeCl}$	174
$\text{C}_2\text{H}_5\text{TeH}$	90	$(\text{C}_2\text{H}_5)_3\text{TeBr}$	162
$\text{C}_3\text{H}_7\text{TeH}$	121	$(\text{C}_2\text{H}_5)_3\text{TeI}$	92
$n\text{-C}_4\text{H}_9\text{TeH}$	157	$(\text{C}_6\text{H}_5)_2\text{Te}_2$	53
$(\text{CH}_3)_2\text{Te}$	82		
$(\text{C}_2\text{H}_5)_2\text{Te}$	137.5		
$(\text{C}_6\text{H}_5)_2\text{Te}$	186 <sub>16.5</sub>		
$\text{Te}(\text{CH}_2)_4\text{CH}_2$	82–83 <sub>12</sub>		
$\text{Te}(\text{CH}_2)_8\text{CH}_2$	166		

### Economic Aspects

Commercial production of tellurium in the U.S. started in 1918, reaching 161,000 lb. in 1951. The average annual production during the preceding decade was 84,000 lb. Producers of tellurium are four refiners of copper: American Smelting & Refining Company, Baltimore, Md.; International Smelting & Refining Company, Perth



Amboy, N.J.; Kennecott Copper Corporation, Garfield, Utah; and United States Metals Refining Company, Carteret, N.J.; and one lead refiner—United States Smelting, Refining & Mining Company, East Chicago, Ind.

As reported by the Dominion Bureau of Statistics, Canadian production started in 1934, reaching 51,000 lb. in 1938. Since then, due to limited demand, recovery dropped to an average of 8000 lb. per year. Canadian producers are Canadian Copper Refiners Limited, Montreal East, Quebec, and International Nickel Company of Canada Limited, Copper Cliff, Ontario.

Other known producers of tellurium are Australia, Germany, and Sweden. Production figures are not available.

Unlike selenium, demand for tellurium falls short of production. As a result, producers' stocks approximate one year's production, while there is on hand several years' supply of unprocessed tellurium-bearing muds and by-products. For the past 20 years, the price remained at \$1.75/lb. with little fluctuation. The price in April 1954 had risen to \$2.10/lb. Tellurium is marketed as lump or a powder. The main outlets are in the rubber industry and in metallurgy, the former consuming about 50,000 lb. per year. The annual consumption of tellurium in chilled iron castings approximates 12,000 lb.

### Uses

**Rubber.** At present, the rubber industry provides the largest single outlet for tellurium, both as the element and as tellurium diethyldithiocarbamate. Powdered tellurium is used as a secondary vulcanizing agent in natural rubber and in GR-S. In many cases, adding 0.5% tellurium increases the rate of vulcanization and improves the aging and mechanical properties of sulfurless and low sulfur stocks. Tellurium is particularly effective when used with tetramethylthiuram disulfide (bis(dimethylthiocarbamoyl)disulfide) and with selenium diethyldithiocarbamate in sulfurless cures. It is used frequently to eliminate porosity in thick-molded sections. Tellurium rubber possesses extreme resistance to heat and abrasion. It is used in all-rubber-jacketed portable cables in mining, dredging, welding, etc., and in conveyor belts for special applications.

Tellurium diethyldithiocarbamate in combination with mercaptobenzothiazole, with or without tetramethylthiuram disulfide, is the fastest known accelerator for butyl rubber. It is used extensively in butyl tubes for bus and similar service and in other butyl applications.

**Ferrous Metallurgy** (27,28,32,33,35,36). The use of tellurium to control the chill depth of iron castings was developed about 1940. Hard, wear-resistant, chilled surfaces were originally produced on gray iron castings by pouring molten iron against a metal surface, a thin layer of white iron forming on rapid cooling. The high cost and the limited life of metal molds led to the development of chill surface by adjusting the carbon, silicon and sulfur content of the molten iron and by adding such carbide-stabilizing agents as chromium and vanadium. The composition of the melt was very difficult to control even under the best operating conditions. This caused a high rejection rate of the castings. These difficulties were eliminated by introducing less than 0.1% tellurium into the melt.

Tellurium is 100–150 times as effective as chromium in producing a given depth of chill. It acts as a powerful carbide stabilizer, minute quantities converting gray

iron to white. As tellurium is very volatile, it is added to the ladle just before pouring. It is added as pellets, powder in aluminum or copper containers, ferrotellurium or copper telluride granules, or in any other convenient form. Alternatively, the mold may be treated by coating the desired areas of the mold surface with tellurium-bearing washes, by surfacing the sand mold with a layer of tellurium-rich sand, etc.

The result is a hard, abrasion-resistant surface, important in many applications of cast iron. The depth of the chill may be controlled by the amount of the added tellurium. The casting invariably shows a sharp demarcation line between the chill and the unchilled region, without an intermediate or mottled zone. Yet, the chilled portion shows excellent resistance to spalling from thermal or mechanical shock. Tellurium-treated iron shows a greater corrosion resistance to sulfuric and hydrochloric acids than untreated, unchilled gray iron. The amount of tellurium added is 0.005–0.1%. About 60% of the additive is lost by volatilization, and excessive addition causes porosity in the castings.

Tellurium-chilled iron is used in mining, automotive, railroad, and other equipment. Tellurium corewashes eliminate troublesome localized shrinkage in castings. These corewashes contain about 25% Te, the balance consists mainly of silica flour with some bentonite.

In manufacturing chilled car-wheels, restriction of the width of the mottled zone within certain limits is desired. A 1:30 tellurium:graphite mixture is consequently used, or approximately 2 g. tellurium and 2 oz. graphite per 1000 lb. iron. The combination of a powerful carbide stabilizer with a powerful graphitizer, controls the fine, dense, mottled transition zone to almost any desired degree.

Tellurium has also been added to cast iron in concentrations up to 0.2% to prevent or retard primary graphitization on subsequent annealing to malleable iron. Concentrations from 0.001 to 0.02% have also been employed. The use of tellurium to control the porosity and to improve the machinability of Cr and Cr-Ni steels has been patented (29). However, selenium is generally preferred for this purpose.

**Copper and Copper Alloys.** A 99.5% Cu–0.5% Te alloy has been marketed for many years (30). Both the electrical and the thermal conductivity of this alloy are about 90% that of pure copper. Its machinability rating is 90, compared with 100 for free-cutting brass and 20 for unalloyed copper.

Unlike lead and other additives, tellurium has no adverse effect upon the hot-working properties of copper. Although the alloy is somewhat less ductile at room temperature than pure copper, it may nevertheless be extensively cold worked. Machining methods are the same as for free cutting brass. Because the copper telluride particles are harder than the lead particles in free-machining brass, carbide tipped tools must be employed. Its use is recommended where high production rate is required without important sacrifice in conductivity. Tellurium-copper has found an outlet in electrical, radio, communications, and similar fields, as well as in welding and cutting tips. It was widely used in military applications during World War II. It is distributed as round rod.

Telnic Bronze is an age-hardening alloy of the nominal composition 98.3 Cu, 1.0 Ni, 0.2 P, and 0.5 Te. It is made in round and hexagonal rods. The machinability rating is 80, the hot-working properties are comparable with high copper commercial bronze and are superior to any lead-containing free-machining copper alloy. Its tensile strength is high, and the electrical conductivity is about one-half that of copper. See Vol. 4, p. 440.

Tellurium-copper (0.5–1% Te) was used in the body of the magnetron, a device invented in Britain for generating very high frequencies essential to radar.

**Lead.** Tellurium-lead containing 0.02–0.1% Te, with or without antimony, was introduced in 1934 (26). Tellurium appears to have a deoxidizing action on lead. The alloy shows very uniform elongation on drawing and preserves fine structure to its breaking point. This is ascribed to the superficial adsorption of tellurium by lead and to the resistant film of lead telluride, which is insoluble in the lead matrix and prevents the growth of lead grains over a wide temperature range.

Adding tellurium confers upon lead useful work- and precipitation-hardening properties, improves resistance to wear, vibration, and mechanical breakdown, and imparts resistance to corrosion. These properties are utilized in marine cable sheathing, where tellurium refines the grain size and improves mechanical properties without impairing corrosion resistance. It successfully replaced tin (1–3% Sn) in the sheathing. Thinner sheaths could be extruded, the extrusion pressure of 0.05% Te lead being about the same as for a 3% Sn alloy. Tellurium is added as a master alloy, a lead-tellurium alloy containing a convenient percentage of tellurium in such quantity as to give a final concentration of about 0.06% Te.

The increased resistance of tellurium lead to corrosion brought about its widespread use in the chemical industry, especially in equipment exposed to sulfuric acid. Tellurium lead has also been used to some extent in lead storage batteries. See also *Lead alloys*.

Adding 0.1–1% Te to pure tin improves the work-hardening properties, the tensile strength, and the creep resistance. Tellurium also controls the structure and improves uniformity and fatigue resistance of babbitt type alloys by restricting the tendency to segregation.

Tellurium has been recommended as an additive to **magnesium** to increase corrosion resistance. The addition reaction is highly exothermic and hence difficult to control.

**Miscellaneous.** Tellurium chloride, as well as tellurium dioxide in hydrochloric acid solution, is used to impart permanent black antique finish to silverware. In the Tainton process of purifying zinc sulfate electrolyte, powdered tellurium has been added to zinc dust to improve the rate and completion of removing cobalt.

Small quantities of tellurium have been consumed in glass and ceramics to produce blue to brown colors. Tellurium has also served as a base for ultramarine-type pigments. A number of patents has been granted for the use of tellurium in petroleum refining and in the manufacture of petroleum chemicals and lubricants. It is not known whether these are being used. High-purity lead telluride has been considered as a transistor and rectifier material, but little work has been done in this direction. Tellurium was widely used for a short time in crystal detectors or dry rectifiers in the early radio sets. It has served as a thermocouple element. In mercury vapor lamps, tellurium gives a color distribution very near to that of daylight, except for a high intensity in the yellow region.

### Bibliography

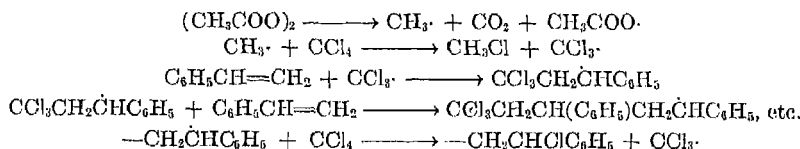
- (1) Benard, F., *Trans. A.I.M.E.*, **106**, 369–97 (1933); **159**, 521–29 (1944).
- (2) Brauer, G., *Handbuch der präparativen anorganischen Chemie*, Enke, Stuttgart, 1951, pp. 335–351.
- (3) Brooks, L. S., *J. Am. Chem. Soc.*, **74**, 227 (1952).
- (4) Duval, C., and Doan, U. M., *Anal. Chim. Acta*, **5**, 569–72 (1951).

- (5) Elkins, H. B., *The Chemistry of Industrial Toxicology*, Wiley, N.Y., 1950.
- (6) Friend, (a) Vol. VII. Pt. II, 1931; (b) Vol. XI, Pt. IV, pp. 166-86.
- (7) Gaev, A. I., Dolzhenko, T. S., and Trutnev, B. V., *Tsvetnye Metal*, No. 10, 64-70 (1938).
- (8) Glemser, O., and Porscher, W., *Z. anorg. Chem.*, **256**, 103 (1948).
- (9) Gmelin, System-Nummer 11, 1940.
- (10) Heberlein, M., *Metal u. Erz*, **30**, 363-6 (1933).
- (11) Henderson, A., and Hardy, H. I., *Industrial Toxicology*, Harper, N.Y., 1949.
- (12) Houben-Weyl, *Die Methoden der organischen Chemie*, Thieme, Stuttgart, 1925-1941.
- (13) *Inorganic Syntheses*, McGraw-Hill, N.Y., Vols. I, II, and III, 1939, 1946, and 1950.
- (14) Latimer, W. M., *Oxidation Potentials*, 2nd ed., Prentice-Hall, N.Y., 1952, pp. 84-87.
- (15) Lenher, V., *Trans. A.I.M.E.*, Paper No. 1198-N, 1923.
- (16) Mason, B. H., *Principles of Geochemistry*, Wiley, N.Y., 1952.
- (17) Mellor, Vol. XI, 1931.
- (18) *Organic Syntheses*, Vols. I-XXXIII, 1941-53.
- (19) Rose, T. K., *The Metallurgy of Gold*, Griffin, London, 1937.
- (20) Schloen, J. H., and Elkin, E. M., *Trans. Can. Inst. Mining Met.*, **49**, 143-90 (1946).
- (21) Schloen, J. H., and Elkin, E. M., *Trans. A.I.M.E.*, **188**, 764-77 (1950).
- (22) Scott, 5th ed., 1939.
- (23) Sidgwick, N. V., *Chemical Elements*, Clarendon Press, Oxford, 1950, pp. 950-94.
- (24) Waddington, R. H., *Can. Metals Met. Inds.*, **3**, 153-58, 190-92, 199 (1940).
- (25) Yost, D. M., and Russell, H., *Systematic Inorganic Chemistry*, Prentice-Hall, N.Y., 1944, Chaps. 8, 9, 10.
- (26) Brit. Pat. 441,524 (June 8, 1934) W. Singleton, W. Huhne, B. Jones, and Goodlass Wall and Lead Industries, Ltd.
- (27) Brit. Pat., 510,757 (Aug. 8, 1939), Meehanite Metal Corp. and O. Smalley.
- (28) Brit. Pat., 552,390 (April 3, 1943), Brit. Cast Iron Research Assoc., E. Morgan and E. Hinchcliffe.
- (29) U.S. Pats., 2,009,713-6 (July 30, 1935), F. R. Palmer (to Carpenter Steel Co.).
- (30) U.S. Pat., 2,027,807 (Jun. 14, 1936), H. L. Burghoff and D. E. Lawson (to Chase Co. Inc.).
- (31) U.S. Pat., 2,076,738 (April 13, 1936), O. C. Martin and C. W. Clark.
- (32) U.S. Pat., 2,250,488-9 (July 29, 1941), C. H. Lorig and D. E. Krause (to Battelle Memorial Inst.).
- (33) U.S. Pat., 2,253,502 (Aug. 26, 1941), A. L. Boegehold (to General Motors Corp.).
- (34) U.S. Pat., 2,258,963 (Oct. 14, 1941), W. G. Woll and R. T. Gore (to International Smelting and Refining Co.).
- (35) U.S. Pat., 2,281,460 (April 28, 1942), O. Smalley (to Meehanite Metal Corp.).
- (36) U.S. Pat., 2,331,886 (Oct. 19, 1943), A. L. Boegehold (to General Motors Corp.).
- (37) U.S. Pat., 2,349,697 (May 23, 1944), N. R. Brierly (to The American Metal Co., Ltd).

E. M. ELKIN AND J. L. MARGRAVE

## TELOMER

A telomer is a polymeric product formed from a monomer and an initiator, R, obtained by a chain-transfer reaction between a radical from a catalyst and some other compound, called a telogen. Polymerization is terminated by addition of X, the other fragment of the telogen. This can be illustrated by the polymerization of styrene with acetyl peroxide as the catalyst, carbon tetrachloride being the telogen (giving  $R = CCl_3\cdot$  and  $X = Cl$ ):



Telomerization is often used to prepare low-molecular-weight polymers. See Fuson, R. C., *Advanced Organic Chemistry*, Wiley, N.Y., 1950, p. 616.

## TEMPERATURE MEASUREMENT

Temperature affects our everyday life and our technical procedures more intimately than any other familiar physical fact. Difference of temperature causes flow of heat from regions of higher to those of lower temperature, and it is this fact that is the basis of our sensory perception of temperature. Temperature determines whether a substance such as water exists as a solid, liquid, or gas; it affects the volume of solids, liquids, and gases; the electrical resistance of conductors; the rate and quality of the emission of heat radiation. It is a controlling factor in most chemical reactions and in the development of desired characteristics in metals. Because of the multiplicity of situations in which a knowledge of existing temperatures is necessary for satisfactory results of operations, the measurement of temperature has attained a high degree of importance in science and industry. See also *Instrumentation*.

**Temperature Scales.** The temperature scales most commonly used, based on the melting point of ice and the boiling point of water, both under the standard pressure of 760 mm. of mercury, are the centigrade (Celsius) and the Fahrenheit. On the centigrade scale these points are assigned the values of 0 and 100, respectively, while on the Fahrenheit scale they are designated as 32 and 212, respectively. Centigrade and Fahrenheit temperatures can be interconverted by the formulas:

$$(^{\circ}\text{C}) = [(^{\circ}\text{F}) - 32]/1.8$$

$$(^{\circ}\text{F}) = 1.8(^{\circ}\text{C}) + 32$$

The following forms of the equations will be found convenient:

$$(^{\circ}\text{C}) + 40 = [(^{\circ}\text{F}) + 40]/1.8$$

$$(^{\circ}\text{F}) + 40 = 1.8[(^{\circ}\text{C}) + 40]$$

Two other scales are extensively used in technical and scientific practice, based on experimental evidence that the volume of a perfect gas would be reduced to zero if its temperature were decreased to  $-273.16^{\circ}\text{C}$ . ( $-459.7^{\circ}\text{F}$ ). This is the lowest possible temperature and is called absolute zero. The absolute or Kelvin temperature of a body is its temperature in centigrade degrees above absolute zero; that is, temperature Kelvin = temperature centigrade  $+273.16$ . The absolute temperature of a body may also be expressed in Fahrenheit degrees. This is called the Rankine temperature scale: temperature Rankine = temperature Fahrenheit  $+459.7$ .

To define temperatures between 0 and  $100^{\circ}\text{C}$ , the 0- and  $100$ -degree points on the stem of a mercury-in-glass thermometer may be determined experimentally and marked. The distance between the marks may be divided into 100 equal intervals, and temperatures may be assumed to be represented by the position of the top of the mercury column on this scale. If the bore of the tube is not perfectly uniform, equal distances on the scale do not represent equal increments of volume of the mercury, and corrections must be determined and applied. Moreover the coefficients of expansion of mercury and of the glass bulb are not uniform over the temperature range, and cause departures from the temperature scale of the perfect gas thermometer. However, before the adoption of the international temperature scale, many laboratories used mercury thermometers divided in this way with which working thermometers were compared. Such thermometers have served a useful purpose, but better

standards of comparison, such as the platinum resistance thermometer are now available.

To avoid linking the temperature scale to the properties of any material, Lord Kelvin proposed the thermodynamic temperature scale, which is based on the theory of the perfect heat engine employing the Carnot cycle. If the engine operates with its source at  $100^{\circ}\text{C}.$  and its sink at  $0^{\circ}\text{C}.$ , a certain amount of work is done during each cycle. If the same engine, operating through a certain temperature interval, does one hundredth as much work as between  $100^{\circ}$  and  $0^{\circ}$ , that temperature interval is 1 degree. This is true, no matter where on the temperature scale this interval is taken, and holds equally well below 0 and above 100. No assumption is made as to the working material. Kelvin showed that this scale corresponds exactly with that which results if a gas thermometer containing a perfect gas were used to determine the 1 degree intervals. See also *Thermodynamics*.

No gas is perfect, and, in interpreting the indications of any actual gas thermometer, it is necessary to allow for the fact that the gas departs from the ideal. With the aid of the gas thermometer and with the ice point (or the triple point of water) and the boiling point of water as the basis, the Kelvin temperatures of boiling, freezing, or triple points of various pure elements or compounds have been established. Once determined, these serve as points of reference in defining the temperature scale below 0 and above  $100^{\circ}\text{C}.$

Until 1927, the only officially recognized international scale of temperature was the centigrade constant-volume hydrogen scale, known as the normal hydrogen scale adopted in 1887 by the International Committee on Weights and Measures. Many other scales were in use in the ensuing years which differed among themselves by amounts that, while usually insignificant industrially, were greater than the limits of experimental error. Some of these scales are still in use in laboratories where it has seemed to be more important to remain consistent with earlier experimental records than to conform to international conventions.

At present, temperatures are expressed officially in terms of the international temperature scale, which was adopted as standard in 1927 by the Seventh General Conference of Weights and Measures and was reaffirmed, with slight revisions, in 1948. The Conference expressed temperatures in centigrade (Celsius) degrees. Certain equilibrium temperatures (fixed points) have been measured with the aid of the gas thermometer with a limit of error of  $\pm 0.05$  deg. C. Table I gives the values assigned to the fixed points which define the international temperature scale from  $-183^{\circ}$  to  $+1063^{\circ}\text{C}.$  Procedures are specified for interpolating between these fixed points, and for extrapolating to temperatures higher than  $1063^{\circ}\text{C}.$

The international temperature scale does not cover values below the oxygen point.

**TABLE I. Fundamental and Primary Fixed Points Under the Standard Pressure of 1,013.250 dynes/cm<sup>2</sup>.**

Temperature of equilibrium between:	Temp., $^{\circ}\text{C}.$
Liquid oxygen and its vapor (oxygen point)	$-182.970$
Ice and air-saturated water (ice point)	0
Liquid water and its vapor (steam point)	100
Liquid sulfur and its vapor (sulfur point)	$441.600$
Solid and liquid silver (silver point)	$960.8$
Solid and liquid gold (gold point)	$1063.0$

Fixed points in this region based on measurements in three different laboratories may be tentatively assigned the following values (where normal hydrogen is a mixture of ortho and para hydrogen):

$n\text{-H}_2$ triple point.....	13.96°K.
$n\text{-H}_2$ boiling point.....	20.37°K.
$\text{O}_2$ triple point.....	54.36°K.
$\text{N}_2$ triple point.....	63.14°K.
$\text{N}_2$ boiling point.....	77.33°K.

A proposal is at present (1954) under consideration that the temperature scale be based on absolute zero and the ice point or the triple point of water as fundamental fixed points. On this scale the ice point would be 273.16°K. and the triple point 273.17°K. The steam point would no longer be fundamental, but on a par with the other fixed points. In scientific literature the centigrade scale would then probably be replaced eventually by the Kelvin scale.

### Measurements Based on Expansion

**Liquid-in-Glass Thermometers.** The most widely used instrument for the measurement of temperatures in the range of temperatures from about  $-170$  to  $+500^\circ\text{C}$ . is the liquid-in-glass thermometer, consisting of a glass tube of small bore with a thin-walled bulb at its lower end, containing sufficient mercury, alcohol, or other fluid to fill the bulb and partly fill the tube. The fluid level in the tube rises and falls with increase or decrease of the temperature of the fluid in the bulb. The upper end of the tube is sealed. It often terminates in a small bulb or reservoir to hold fluid which rises to the top of the tube when the thermometer is overheated, thus safeguarding against bursting. Graduations, engraved on the wall of the tube or on an associated scale, are calibrated in terms of temperature, corresponding to the level of the top of the liquid column.

Mercury is the liquid commonly used for temperatures above its freezing point ( $-39^\circ\text{C}$ .). For lower temperatures, an organic liquid such as an alcohol having a low freezing point must be used. When the mercury thermometer is to be used to measure high temperatures, the space above the mercury column is filled with nitrogen at a pressure of from 30 to 300 p.s.i. to prevent evaporation or boiling of the mercury that would cause errors in calibration. The liquid-in-glass thermometer is suitable only for visual readings and is not an easily made recording, except to the extent that maximum and minimum temperatures experienced since the last resetting can be indicated by iron floats moved by the mercury column and left by it at the highest or lowest position attained.

The glass of the thermometer must be selected for stability, and must be very thoroughly annealed. The bulb, at high temperatures and pressures, is liable to permanent increase of volume, causing the thermometer indication to be too low.

The most accurate mercurial thermometers are graduated and calibrated for total immersion, that is, with all the mercury, including that in the stem, at the temperature being measured. If part of the mercury column extends outside the region in which the temperature is being measured, a correction must be applied to the reading, based on the length in degrees of the emergent column, on the difference in temperature between the emergent column and the bulb, and on the relative expansion of mercury and glass.

Table II, reproduced from *Natl. Bur. Standards Circ.*, 8, 4th ed., states the graduation intervals appropriate for the temperature ranges listed, the tolerances allowed by the National Bureau of Standards in issuing certificates, the accuracies which may be expected from the ranges and types represented, and the decimal figure to which the corrections are stated on the document.

TABLE II. Tolerances for Total Immersion Mercurial Centigrade Thermometers.

Temp. range, °C.	Graduation interval, °C.	Tolerance, °C.	Accuracy, °C.	Corrections stated to
Thermometers for low temperature				
-35 to 0	1 or 0.5	0.5	0.1-0.2	0.1
-35 to 0	0.2	0.4	0.02-0.05	0.02
Thermometers not graduated above 150°C.				
0 up to 150	1 or 0.5	0.5	0.1-0.2	0.1
0 up to 150	0.2	0.4	0.02-0.05	0.02
0 up to 100	0.1	0.3	0.01-0.03	0.01
Thermometers not graduated above 300°C.				
0 up to 100	1 or 0.5	0.5	0.1-0.2	0.1
Above 100 up to 300	1 or 0.5	1.0	0.2-0.3	0.1
0 up to 100	0.2	0.4	0.02-0.05	0.02
Above 100 up to 200	0.2	0.5	0.05-0.1	0.02
Thermometers graduated above 300°C.				
0 up to 300	2	2	0.2-0.5	0.2
Above 300 up to 500	2	4	0.5-1.0	0.2
0 up to 300	1 or 0.5	2	0.1-0.5	0.1
Above 300 up to 500	1 or 0.5	4	0.2-0.5	0.1

The values given in Table II apply only to the highest grade of mercurial thermometers which are the only ones admitted for certification by the National Bureau of Standards. A typical chemical thermometer with a range from  $-5$  to  $+150^{\circ}\text{C}$ . graduated in 1-degree intervals has a tolerance of  $\pm 1$  degree.

**Beckmann Thermometer.** The Beckmann differential thermometer has a scale about 1 ft. long, with a total range of 5 or 6 deg. C. in 0.01-degree divisions. It is so constructed that a portion of the mercury in the bulb can be transferred to a reservoir so as to bring the top of the mercury column into the graduated section, for the various temperature ranges in which differences may be measured. It is used only for measuring differences in temperature. The accuracy attainable is estimated to be between 0.002 and 0.005 degree in the measurement of any interval within the limits of the scale.

**Bi-metallic strip thermometers** consist of a strip made up of two metals with widely differing coefficients of thermal expansion, such as Invar and brass, welded or brazed together face to face throughout their length. The strip may be nearly straight, or it may be formed into a spiral to secure greater sensitivity. A rise in temperature changes the curvature of the strip, since the brass increases in length more rapidly than the Invar. If one end is fixed, a pointer linked to the free end can be caused to move over a scale calibrated in temperature, or a pen can be made to move across a moving chart so as to record the temperature. Bi-metallic strips are also very



commonly used to actuate electrical contacts so as to control the temperature of rooms, air baths, or ovens.

The response to temperature changes is nearly linear. Within its accepted temperature range (not above 150°C. when brass is used, considerably higher when a nickel-chromium alloy replaces the brass), errors inherent in the strip are slight. Very appreciable errors may be introduced in the mechanical linkage. In one form the bimetallic strip is a spiral inside a slender metal tube, and the indicating pointer moves over a circular calibrated scale, coaxial with the tube. It can replace the mercury thermometer for many uses.

### Filled-System Thermometers

**Gas-Filled Thermometers.** The constant-volume gas thermometer, mentioned in connection with the establishment of the thermodynamic temperature scale, belongs to the category of gas-filled thermometers and is the most precise of this type. It is not used outside of standardizing laboratories because of its complexity and size. For industrial use a gas-pressure thermometer consists of a pressure-measuring element of the Bourdon tube type (see Vol. 11, p. 92) connected by capillary tubing to a bulb which is exposed to the temperature to be measured. The system is filled under pressure with an inert gas, usually nitrogen. Since the pressure of a gas in a closed container is proportional to its absolute temperature, the measuring element can be calibrated in temperature degrees, with a uniformly divided scale. Since the gas in the measuring element and in the connecting tube is not at the temperature of the bulb, the bulb volume must be large so that the errors introduced by differences of temperature of the pressure-measuring element and the capillary may be insignificant. It should have at least forty times the volume of the rest of the system. Because of this fact, and because of the lag in transmitting pressure changes through the capillary, the length of the latter is limited to a maximum of 200 ft., and is preferably much less.

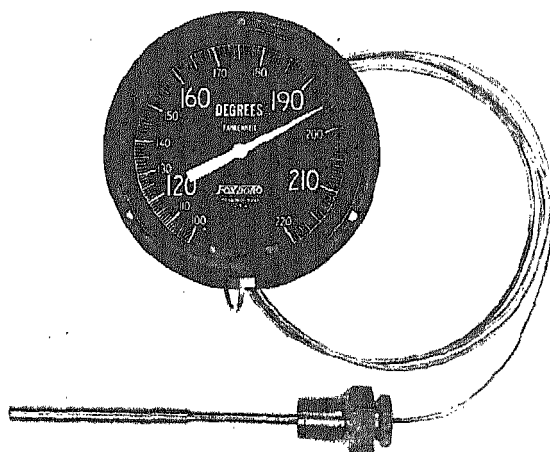
The initial pressure in the gas thermometer is usually between 150 and 500 p.s.i. The torque produced is then ample to operate a recording pen when the scale span is 400 deg. F. or more. Scale spans of less than 120 deg. F. are not recommended. With a scale span of 400 deg. F. or more, the reproducibility of readings is of the order of  $\pm \frac{1}{4}\%$  of the span. The response time tends to be long, partly because of the necessity of transmitting pressure changes through a tube of fine bore and partly because of the large volume and poor thermal conductivity of the nitrogen. To give sufficient volume, the bulb usually has a diameter of  $\frac{7}{8}$  in., resulting in slow response. Response time may be decreased by securing the desired volume by the use of a long,  $\frac{1}{4}$ -in. tube, usually in the form of a 2-in. coil.

Temperature may be indicated by a pointer moving over a graduated scale, or recorded on a circular chart by a pen actuated by the pressure measuring element. Scale spans for the recorders are rarely less than 200 deg. F., but for indicators the range may be narrower.

Variations in barometric pressure are normally not large enough to affect the indications appreciably, but major changes in altitude must be corrected for in calibration.

Gas-pressure thermometers are used at temperatures between  $-450^{\circ}\text{F.}$  and  $+1000^{\circ}\text{F.}$ , which fall partially or entirely outside the limits for vapor-pressure systems, and for applications where their lesser accuracy and larger bulb size do not, for the particular application, outweigh the higher cost of the liquid-expansion type.

**Vapor-Pressure Thermometers.** Vapor-pressure thermometers make use of the fact that, in a closed vessel which contains nothing but a liquid and its vapor, the liquid only partially filling the enclosure, the pressure is dependent only on the material of the liquid and on its temperature. Very extensive use is made of this relationship between vapor pressure and temperature in the measurement and recording of industrial temperatures. The vapor-pressure thermometer (Fig. 1) resembles the gas-pressure thermometer in consisting of a bulb, a connecting tube of fixed length, usually from 5 to 250 ft. long, and a pressure-sensitive element (Fig. 2). The bulb is partly filled with a fluid with a boiling point low enough to produce a working pressure of 75 to 500 p.s.i. in the temperature range to be covered. The upper end of the range must be lower than the critical point of the liquid. Various liquids such as methyl chloride,



*Courtesy The Foxboro Company*

Fig. 1. Vapor pressure thermometer.

sulfur dioxide, ether, ethyl alcohol, and toluene are used, selected for suitable vapor pressure vs. temperature relationships, inertness to metals in the system, and availability in a pure form. Such liquids are available covering a range from  $-180$  to  $300^{\circ}\text{C}$ .

Vapor pressure increases with temperature more rapidly as the temperature rises, so that the vapor pressure - temperature curve is nonlinear, and charts graduated in temperature have their degree marks much farther apart at the upper end of the range than at the lower. A recorder with a chart range from  $10$  to  $100^{\circ}\text{C}$ . may have graduations  $2$  deg. C. apart from  $10$  to  $40^{\circ}\text{C}$ . and only half a degree apart from  $40$  to  $100^{\circ}\text{C}$ . Readability is poor at the low end of the range. The reproducibility of vapor-pressure thermometers is of the order of  $\pm 1\%$  and in some cases considerably better.

The level of the bulb with respect to the pressure-measuring device is important because, if the temperature of the connecting tubing is below the temperature of the bulb, filling liquid will condense in the connecting tubing. The pressure-measuring device is subjected to the vapor pressure in the bulb plus hydrostatic head of this column of liquid if the bulb is above the measuring device, or to the vapor pressure in the bulb minus the hydrostatic head if the bulb is below the measuring device. If the operating temperature of the bulb will be higher than the temperature of the pres-

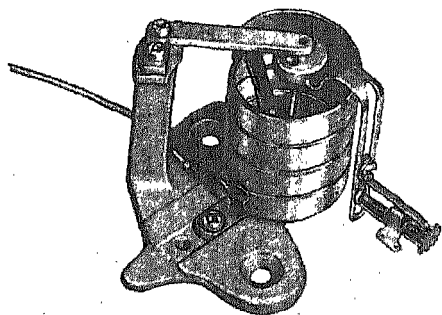
sure-measuring device, the instrument is calibrated for a definite difference of level. Corrections must be applied if the elevation of the bulb is changed.

A major weakness in this type of measuring system is the upset due to shifting of the liquid from bulb to pressure element or reverse as the measured temperature crosses the temperature of the instrument.

**Liquid-Expansion Thermometers.** In a liquid-expansion thermometer the system is completely filled with a suitable liquid and consists of a bulb connected by capillary tubing to an element in the shape of a Bourdon helix or spiral and located in the case of the instrument. An increase in temperature causes expansion of the liquid, the element uncoils to provide the increased volume, and the instrument reading rises. The filling pressure selected must be such that the boiling point of the liquid is appreciably higher than the top temperature that the system is to measure. Temperatures can be measured from  $-175^{\circ}\text{C.}$  to  $+300^{\circ}\text{C.}$  (and  $550^{\circ}\text{C.}$  for mercury). Although the volume changes are relatively small, the forces exerted can be great for actuating the element, and therefore this type of measurement is considered good for controllers requiring a high degree of stability. Reproducibility in the order of  $\frac{1}{4}$  of 1% can be expected.

The major source of error in this type of measurement is the thermal expansion of the liquid not in the bulb. When the tubing length is short, the error is mostly in the Bourdon element, and a bimetal correction element is normally placed in the case to compensate for this error. When the capillary tubing is long either one of two methods is used for correction. (1) A central wire is placed in the capillary tubing and runs its full length; this wire has a relative expansion coefficient that corrects for the change in volume of the liquid. Normally this is used only in mercury-filled systems. (2) A second capillary tube, closed off at the end rather than having a bulb attached, is run parallel to the capillary from the bulb and operates an identical helical Bourdon in the instrument case, so linked with the original element that any expansion in this correction capillary end element subtracts from the other system and thereby corrects for the expansion everywhere except in the measuring bulb.

Any thermal expansion of the bulb is automatically included in the calibration of the system. The thermal expansion of the capillary tube and sensitive element are completely negligible.



*Courtesy The Foxboro Company*

**Fig. 2. Pressure-sensitive element.**

### Electrical Methods

**Resistance Thermometer.** The sensitive element of a resistance thermometer (see Fig. 3) is a carefully mounted and protected wire of a pure metal, typically of platinum, with means provided for detecting and measuring changes in its resistance. The relationship between the resistance and the temperature (between 0 and  $+630^{\circ}\text{C.}$ ) of a coil of pure platinum wire is given by the equation:

$$R_t = R_0 (1 + At + Bt^2)$$

where  $R_t$  is its resistance at temperature  $t$ ,  $R_0$  is its resistance at  $0^\circ\text{C}$ ., and  $A$  and  $B$  are constants which are computed from measurements of  $R_t$  at the ice point, steam point, and sulfur point. For measurements of temperature below  $0^\circ\text{C}$ . a third constant must be determined with the aid of a measurement of  $R_t$  at the oxygen point. Values of  $t$  computed with the aid of the above formula from precise measurements of  $R_t$  are found to agree with the thermodynamic scale within the limits of accuracy attainable with the constant-volume gas thermometer.

For this reason, and because of the advantageous physical properties of platinum, the platinum resistance thermometer was chosen as the standard for determining temperatures between the fixed points of the international temperature scale, from the oxygen point ( $-183^\circ\text{C}$ .) to the antimony point ( $630.5^\circ\text{C}$ .). Tables are prepared for the individual thermometer giving  $t$  vs.  $R_t$ , so as quickly to convert measured values of  $R_t$  to temperature of the platinum wire. With a suitably calibrated resistance thermometer measurements can be made with an accuracy of  $0.01^\circ\text{C}$ ., and changes in temperature of  $0.001^\circ\text{C}$ . are measurable.

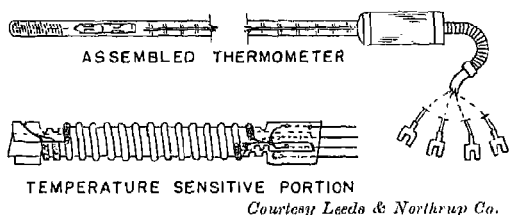


Fig. 3. Platinum resistance thermometer, Meyers type.

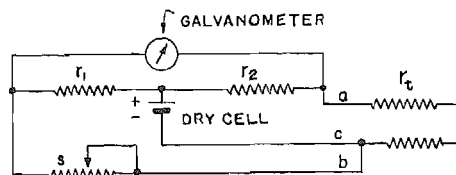


Fig. 4. Three-lead resistance thermometer bridge.

The value chosen for  $R_0$  is usually approximately 25.5 ohms. Platinum increases in resistivity by about  $0.39\%$  of its resistivity at  $0^\circ\text{C}$ . per deg. C. rise in temperature. At  $100^\circ\text{C}$ . the value of  $R_t$  will therefore be about 35.5 ohms, an increase of 10 ohms, or of 0.1 ohm per degree. To measure to  $0.01^\circ\text{C}$ . with an error of less than  $1\%$  it should be possible to measure  $R_t$  to the nearest  $0.00001$  ohm. Such resistance measurements require measuring equipment of the highest attainable precision, maintained at a uniform temperature and carefully calibrated. The measuring instrument may be either a specially designed Wheatstone bridge or a precise potentiometer. The Mueller bridge is commonly used for precise measurements, although equally good precision can be attained with a suitable potentiometer.

It is important that the resistance is measured by a method which gives the resistance of the platinum coil, independent of lead resistance. For the potentiometric method of measurement, two leads are attached to each end of the platinum coil. One of these is a current and the other a potential lead. The potentiometer measures the potential drop of a known current through the platinum coil. In the bridge method of measurement, only three of these leads are in use at a given setting. Figure 4 is a simplified diagram, showing the three-lead connection.

The ratio coils,  $r_1$  and  $r_2$ , give an accurate 1:1 ratio,  $S$  is a standard resistor, adjustable in very fine steps; and  $R_t$  is the thermometer winding. Leads  $a$  and  $b$  are in the thermometer and in the standard arms, respectively. They are made as nearly identical as possible and are mounted in a common sheath, usually together with lead  $c$ , which is a battery lead. When the bridge is balanced, since  $r_1 = r_2$ ,

$S + b = R_t + a$  and, since  $a = b$ , no matter what their common length or temperature,  $S = R_t$ . The fourth lead (not shown) attached at the same end of the winding as the  $a$  lead makes it possible, by suitable commutation of connections, to correct for any residual lack of equality in the leads.

Platinum is much used in industrial resistance thermometers, over the temperature range from about  $-50$  to  $550^{\circ}\text{C}$ . Metal tubes protect the windings from damage, and are so arranged as to allow rapid heat interchange between the winding and the medium in which the tube is placed. A precision of  $0.1$  deg. C. is attainable.

Nickel resistance thermometers (see Fig. 5) have had considerable use. They range in value of  $R_0$  from 10 to 1000 ohms, the higher values being used to swamp out error due to varying lead and contact resistance, particularly in circuits where only two leads are used. In this case the measuring circuit is often a Wheatstone bridge which is balanced for one particular temperature of the thermometer. Changes in temperature unbalance the bridge, and the unbalance current is used as a measure of the temperature. The thermometer can thus be made direct-reading on the dial of a current meter, just as conveniently as is the case for pressure-type thermometers. In more precise industrial installations, in which bridge balance is secured either manually or by means of an automatically balancing recorder, three-lead thermometers

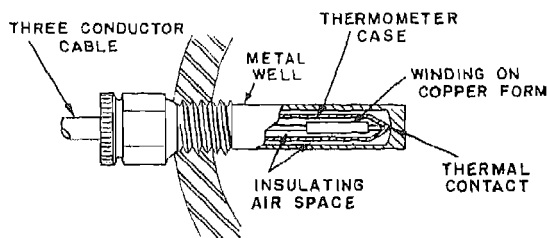


Fig. 5. Nickel resistance thermometer.

are used. In this application, copper is much used in place of platinum or nickel at temperatures below  $300^{\circ}\text{C}$ . Its temperature vs. resistance curve is almost exactly linear from  $-50$  to  $+200^{\circ}\text{C}$ . Because the low resistivity of copper makes a 100-ohm thermometer too bulky, the value of  $R_0$  for copper thermometers is usually about 10 ohms.

Resistance thermometers in industrial and laboratory applications are useful over nearly the same temperature range as the "mechanical" thermometers. They have the advantages of greater sensitivity and precision and of being adapted to much greater distance between sensitive element and measuring instrument. With the aid of a simple switching device, a single conveniently located, manually or automatically balanced measuring instrument can be used to measure the temperatures at many widely distributed and often difficultly accessible points in a building or in a production process.

The sensitive element must be thoroughly protected against damage by the surrounding medium whose temperature is being measured, and must often be provided with a protecting tube or well, usually of metal, in addition to the closed tube which is an integral part of the thermometer. This increases the time lag in coming to temperature equilibrium with the surroundings, and requires that attention be given to

depth of immersion, and contact between tube and well, to insure that the temperature of the winding is unaffected by heat losses along the protecting tube.

The resistance thermometer is well adapted to the measurement of small temperature differences, such as the depression of the freezing point of a nominally pure substance by the presence of impurities.

**Thermoelectric Thermometers (Thermocouples).** If two wires of different materials are in good electrical contact at a pair of ends and the junction is heated, an electromotive force (e.m.f.) is developed. The two wires form a thermocouple. If the other two ends are joined through a current-detecting instrument, it is found that a current flows in this closed circuit as long as the heated junction is hotter than the other (reference) junction. If the reference junction is kept at a constant known temperature, the e.m.f. generated depends upon the temperature of the hot junction and can be used as a measure of this temperature. This constitutes a thermoelectric thermometer. If the circuit has a constant resistance, the current can be used as a measure of the e.m.f. The current-measuring instrument can be graduated in millivolts, or, for a given thermocouple and reference junction temperature, in temperature of the measuring junction. This is the millivoltmeter or deflection method which presupposes that the resistance of the circuit remains unchanged. The e.m.f. may preferably be measured by balancing it against a known e.m.f. by means of a potentiometer (see *Potentiometry*). In this case no current flows in the thermocouple circuit and the e.m.f. measurement is independent of the circuit resistance.

The following combinations of materials are in most common use for thermocouples:

*Platinum* vs. an alloy of 90% *platinum* – 10% *rhodium*. It is usable at a temperature as high as 1600°C. and is suitable for continuous use at temperatures from 0 to 1550°C. This thermocouple was adopted by the General Conference of Weights and Measures in 1927 as the means for defining the international temperature scale from the melting point of antimony to the melting point of gold (630.5–1063°C.). It has a thermoelectric power of about 10 microvolts per deg. C. and is extremely stable and reproducible when properly used. It must never be exposed to reducing atmospheres at temperatures above 500°C. for it deteriorates as a result of gas absorption and of deposition on it of metals reduced from the oxides of the protecting tube and ceramic insulators.

*Copper* vs. *Adam's constantan* (an alloy of approximately 57% copper and 43% nickel with fractional percentages of manganese and iron) is usable at temperatures from –250 to 300°C., and for short periods up to 400°C. From –200 to –100°C. the thermoelectric power is about 20 microvolts per deg. C., and from 200 to 300°C. about 55 microvolts per deg. C. The copper-constantan thermocouple is much used in laboratory measurements at low temperatures. It fails at temperatures above 300°C. because of the oxidation of copper.

*Chromel* (90% nickel, 10% chromium) vs. *Alumel* (94% nickel, 3% manganese, 2% aluminum, 1% silicon) is usable between –200 and 1260°C., but its most useful range is above 700°C. Its thermoelectric power over this range is about 40 microvolts per deg. C. Reducing atmospheres and atmospheres containing sulfur dioxide or hydrogen sulfide are injurious, and the couple deteriorates rapidly in atmospheres containing hydrogen or carbon monoxide. In oxidizing atmospheres it has a long life, and is the most useful of the base metal thermocouples in measuring temperatures above 800°C.

*Iron* vs. *Constantan*. Iron for thermocouples is an alloy with small, but definite

amounts of manganese, copper, nickel, and carbon, and minimum amounts of chromium, sulfur, phosphorus, and silicon. The constantan differs slightly from Adam's constantan. The iron-constantan thermocouple is usable between  $-190$  and  $870^{\circ}\text{C}.$ , in either oxidizing or reducing atmospheres. In reducing atmospheres, it can be used up to  $1000^{\circ}\text{C}.$ , but the e.m.f. vs. temperature relation is not well established above  $900^{\circ}\text{C}.$  Above  $300^{\circ}\text{C}.$ , its thermoelectric power is about 60 microvolts per deg. C. Below  $0^{\circ}\text{C}.$  it is about 40 microvolts. Industrially, this is the most commonly used thermocouple.

In addition to the four mentioned above, many other thermocouple combinations are in current use. These include platinum vs. platinum, 13% rhodium; Chromel vs. constantan; Chromel vs. white gold (gold, 10% nickel); Chromel vs. stainless steel; nickel vs. nickel-molybdenum; tungsten vs. graphite; graphite vs. silicon carbide; tungsten vs. iridium.

The e.m.f.-temperature relationships of the four principal varieties of thermocouples have been determined and are published in a convenient tabular form in references (7,8).

With the aid of such tables, the temperature of the measuring junction can be determined by a measurement of the e.m.f. generated when the reference junction is held at the freezing point. The precision attainable depends upon the precision of measurement of the e.m.f. and the accuracy upon the agreement of the particular thermocouple used with its standard table. Commercial base metal thermocouples from stock are guaranteed to match the corresponding table to  $\pm 1.0\%$  of the measured e.m.f. at temperatures above  $260^{\circ}\text{C}.$  and  $\pm 33$  microvolts below  $260^{\circ}\text{C}.$  With selected and calibrated thermocouples, the agreement may be better than 0.1%, and correspondingly accurate temperature measurements can be made if the potentiometric method of measuring e.m.f. is employed.

In the case of the platinum vs. platinum - 10% rhodium thermocouple, used for reproducing the international temperature scale between  $630.5$  and  $1063^{\circ}\text{C}.$ , the individual thermocouple is calibrated by determining its e.m.f. with its reference junction in melting ice and its measuring junction successively at the freezing points of antimony, silver, and gold. The known values of  $t$  and the measured value of  $e$  are substituted in the formula:

$$e = a + bt + ct^2$$

and the constants  $a$ ,  $b$ , and  $c$  are computed. Then the temperature  $t$  in degrees C. corresponding to any measured value of  $e$  can be computed from the formula, which defines the temperature scale between  $630.5$  and  $1063^{\circ}\text{C}.$ , but it does not necessarily hold precisely outside this range. To illustrate the magnitude of these constants and the precision with which they are determined at the National Bureau of Standards, the following values were given for a particular thermocouple:  $a = -328.86$ ,  $b = +8.29990$ ,  $c = 0.00161064$ ,  $e$  being expressed in microvolts. Below  $630.5^{\circ}\text{C}.$  the thermocouple may be calibrated by comparison with a standard platinum resistance thermometer in suitable fluid baths, while above  $1063^{\circ}\text{C}.$  it may be calibrated in a black-body furnace against a standard optical pyrometer.

*Structure of Thermocouples.* The measuring junction of the thermocouple is preferably welded or hard-soldered. The wires may be twisted together for two or three turns before welding to reduce strains on the weld, but it should be remembered that electrical contact of the wires, except at the weld will introduce an error if there is a

temperature difference between the weld and the point of contact. In the laboratory, the thermocouple wires may terminate in ice baths where they are joined to copper leads making connection to the millivoltmeter or potentiometer, thus maintaining the reference junction temperature at the ice point. In most industrial applications the maintenance of ice baths is impractical and means must be provided in the measuring instrument to compensate its indication for the difference between the actual temperature of the reference junction and the ice point (see Fig. 6).

*Extension Leads.* The indicating or recording instrument must frequently be placed at a considerable distance from its thermocouple. The thermocouple wires are not suitably insulated and are often too large to be put in suitable conduits. Extension lead wires are provided for this purpose, properly insulated, and of suitable size. Preferably the extension leads are of the same materials as the thermocouple wires to which they are joined. In the case of platinum vs. platinum-rhodium this is

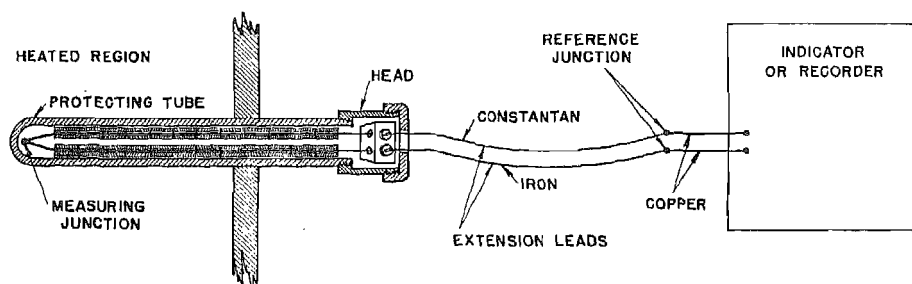


Fig. 6. Thermoelectric thermometer.

too expensive, and leads of copper and of an alloy of nickel and copper are used. These have approximately the same thermoelectric characteristics as the thermocouple wires to which they are joined in the limited temperature range to which the reference junctions will be exposed.

*Protecting Tubes.* Although in some cases the thermocouple may be inserted in the region where the temperature is to be measured, such as an oil bath, without a protecting covering, in general the wires are insulated from each other and they are placed in a protecting tube. The insulating and tube materials used depend upon the temperature and the nature of the medium. For temperatures below 100°C. enameled wires may be used. For temperatures up to 500°C. a glass fiber insulation may be used. For use from the lowest to the highest temperatures the insulation may be ceramic tubes or beads. The protecting tube may be of metal, ceramic, graphite, etc., depending upon the temperature to be measured and the nature of the atmosphere or liquid in which it is placed. The function of the protecting tube is to keep the thermocouple in an atmosphere of dry air and to shield it from mechanical and chemical damage. Many varieties of protecting tubes are available, and the manufacturer of thermocouples should be consulted as to which should be used in a particular application.

*Pipe-Type (Coaxial) Thermocouples.* Thermocouples are often constructed in which one element, for example iron, is in the form of a pipe while the other (constantan) is an insulated wire inside the pipe and welded to a plug that closes the lower end of the pipe. The iron pipe thus performs the function of the protecting tube and, if



coated with a thin film of chromium or a nickel-chromium alloy, is resistant to oxidation.

*Uses.* Thermocouples were first developed for use in pyrometry, that is, the measurement of temperature higher than 500°C., but they are competitive with resistance thermometers and the various expansion and pressure types of thermometers in the lower ranges of temperature. They are competitive with radiation methods of measuring temperature up to about 1500°C. They are well adapted to the recording and control of temperatures throughout this wide range, and are depended upon with a minimum of personal attention in many widely diversified fields of industry.

*Precautions.* Thermocouples should be made of wires obtained from reputable sources and carefully tested for match with the appropriate e.m.f. vs. temperature table. The installed thermocouple should be checked at suitable intervals. If a permanent thermocouple installation is to be made in a plant, lead wires should be run in grounded metal conduits. The lead wires themselves should have weatherproof, heat-resistant insulating coverings. All joints except at the thermocouple head should be soldered and taped. The leads should not be run through hot regions, for example, over the roof of a poorly insulated furnace. Where more than one thermocouple is to be monitored by a single measuring instrument, the selector switch should be of the double-pole variety, so that both thermocouple leads are disconnected from the circuit when transferring to another thermocouple.

### Optical Pyrometry

There is an intimate and consistent relationship between the temperature of any body and the quantity and quality of the thermal radiation that it emits. Three general characteristics of thermal radiation are made use of in temperature measurements; color, quantity, and brightness. The optical pyrometer makes use of the third of these; the brightness of radiation in a very narrow band of wave lengths emitted by a source, the temperature of which is to be measured, is matched visually against the brightness, in the same band, of a calibrated source.

If the source is a perfect radiator, a so-called blackbody, a relation exists between the brightness  $J_{\lambda T}$  of the source in this narrow band, the mean effective wave length  $\lambda$  of this band, and the absolute temperature  $T$  of the source, which is expressed closely by Wien's spectral distribution law:

$$J_{\lambda T} = c_1 \lambda^{-5} \exp\{c_2/\lambda T\}$$

Planck's modification of the spectral distribution law:

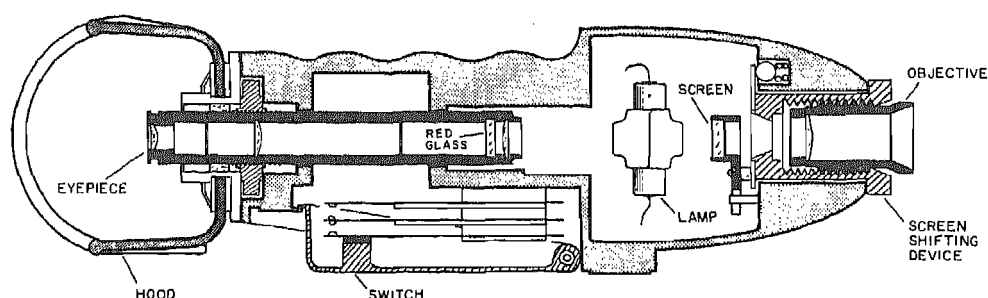
$$J_{\lambda T} = c_1 \lambda^{-5} \exp\{(c_2/\lambda T) - 1\}$$

is exact. In these expressions  $c_1$  and  $c_2$  are physical constants which can be determined experimentally by various independent methods.

With the aid of the optical pyrometer, these laws can be used to extrapolate the international temperature scale beyond the range of gas thermometry, in agreement with the theoretical thermodynamic scale. Wien's law is sufficiently precise for visible wave lengths up to at least 1800°C. and is mathematically more convenient to handle than the more exact Planck's law.

The optical pyrometer which has been used in the determinations of high temperatures such as the melting points of platinum, molybdenum, or tungsten is of the

disappearing filament type. A telescope (see Fig. 7) is focused on the incandescent object whose temperature is to be measured. The filament of a highly evacuated tungsten lamp is located in the focal plane of the objective of the telescope. The eyepiece is focused on this plane, and includes a red glass filter which transmits only a narrow band of visible wave lengths centered at 0.65 microns. The tungsten filament is heated by a current from a battery, the current being controlled by a rheostat and measured, preferably by a potentiometric method. To make a measurement the superimposed images of source and filament are matched in brightness by adjusting the filament current. When the brightnesses are equal, the filament disappears against the background of the image of the source. The filament appears as a dark or a bright line, depending upon whether it is less bright or more bright than the image of the source. The eye is very sensitive to difference in brightness, and, since the brightness of an object increases from 10 to 20 times as fast as its absolute temperature,



*Courtesy Leeds & Northrup Co.*

Fig. 7. Optical pyrometer telescope.

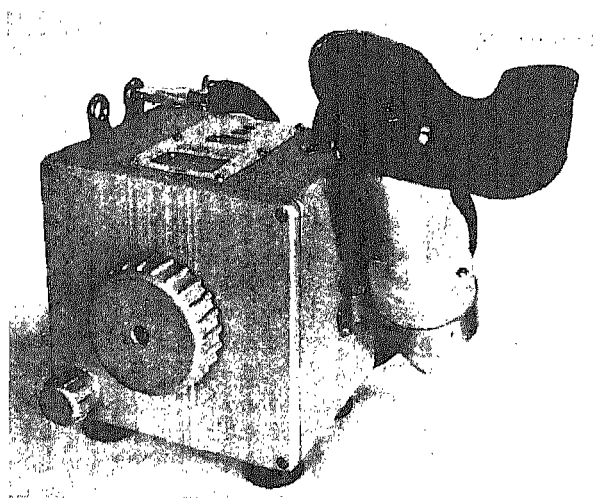
a 1% error in brightness match involves only from 0.05 to 0.1% error in temperature. When the disappearance of the filament has been secured, the current is read; or, if the current scale is graduated in terms of temperature, the temperature is read directly.

Figure 8 represents a modern optical pyrometer widely used both in laboratory and in industrial work. Such an instrument is calibrated by observing the current required to secure disappearance when the source is a blackbody which can be held at various known distributed temperatures. One of these may be the gold point, 1063°C., and another the silver point, 960.8°C. Other temperatures of the blackbody furnace may be determined by means of a standard platinum vs. platinum - 10% rhodium thermocouple. The scale of current vs. temperature is secured by interpolation between these measured points. The practical lower end of the temperature range of the optical pyrometer is about 750°C., since at lower temperatures the image brightness is too faint to make accurate matching possible. The upper end of the range of the instrument as described is about 1250°C. At higher temperatures the eye is dazzled by the brightness.

To measure and to define higher temperatures, it is necessary to resort to screening of the radiation from the source, so as to reduce the apparent brightness of the source sufficiently that it can be matched in the calibrated range of the filament. A screen which transmits a known fraction of the radiation is a rapidly rotating sector disk placed between the objective lens and the filament. With the aid of Wien's spectral distribution law it can be shown that the following relationship holds:

$$\frac{\lambda \ln \tau}{c_2} = \frac{1}{T_2} - \frac{1}{T_1} = A$$

where  $\lambda$  is the mean effective wave length transmitted by the red filter,  $\tau$  is the fraction of the light from the source transmitted by the screen,  $c_2$  is a known constant (14,380 micron degrees),  $T_1$  is the absolute temperature observed through the screen as measured on the scale of the pyrometer, and  $T_2$  is the actual temperature of the source. For a given screen and red glass filter,  $A$  is a constant, which is usually expressed in *mireds* (negative micro-reciprocal degrees) and is computable from the known values of  $\lambda$ ,  $\tau$ , and  $c_2$ . To determine a temperature  $T_2$  above 1063°C. a screen is used which reduces the brightness sufficiently to make  $T_1$  fall in the calibrated range, below 1063°C.



Courtesy Leeds & Northrup Co.

Fig. 8. Optical pyrometer.

Then, measuring  $T_1$ ,  $T_2$  can be computed. By this method temperatures have been determined on the international temperature scale (thermodynamic scale) for freezing points up to that of tungsten, 3380°C. For temperatures above about 1800°C. the discrepancy between the Wien and the Planck spectral distribution laws becomes significant, and the latter is used in computing the freezing points.

Outside the standardizing laboratory the sector disk is impractical and is replaced with an absorbing glass screen. The  $A$  value of the screen is determined by measuring through it the apparent temperature  $T_1$  of a blackbody source at known temperature  $T_2$ , such, for example, as the freezing point of platinum. Suppose that the reading on the temperature scale of the calibrated pyrometer, when freezing platinum in a blackbody furnace is the source, is found to be 1000°C., or 1273°K. The freezing point of platinum is known to be 1760°C. or 2033°K. Thus:

$$A = \frac{1}{2033} - \frac{1}{1273} = -0.000294 \text{ or } 294 \text{ mireds}$$

If the screen glass has the proper transmission characteristics,  $A$  is constant for all values of  $T_2$ , and for each temperature on the low-range scale the corresponding tem-

perature of a source observed through the screen can be computed. A high-range scale can thus be laid out paralleling the low-range scale, to be used when measuring temperatures above those covered by the low-range scale. Limits of error are such that measurements accurate within a tolerance of  $\pm 4$  deg. C. up to  $1225^{\circ}\text{C.}$  and of  $\pm 8$  deg. C. up to  $1750^{\circ}\text{C.}$  are easily made with an intelligently used and properly maintained industrial optical pyrometer. Even inexperienced observers are consistent in their readings within 5 deg. C. at temperatures up to  $1750^{\circ}\text{C.}$  and experienced observers in a darkened room are consistent to better than 1 deg. C.

Other variable current optical pyrometers use the voltage drop through the filament, or the resistance of the filament, as a measure of the temperature of disappearance.

**Optical Wedge Type.** The optical pyrometer described above is the type used in establishing the international temperature scale above the gold point and is widely used in laboratories and in industry. Another type, permitting lighter and more compact construction, operates with the filament current always at a fixed value, as indicated by the pointer of a current indicator. Disappearance of filament is secured by setting an absorbing wedge interposed between the objective lens and the filament, thus reducing the apparent brightness of the source to that of the filament. A calibrated scale moves with the wedge and indicates the source temperature against an index line. The precision attainable is not so good as with the instrument in which the filament current is varied and is measured potentiometrically.

**Nonblackbody Temperatures.** The blackbody is so called because it absorbs all the radiation incident on it, reflecting none. A blackbody at temperatures below incandescence is therefore perfectly black. At higher temperatures it is luminous, and at any given temperature it emits radiation at a greater rate than any nonblackbody, in accordance with Kirchhoff's law of radiation, which states that any body which is a good absorber of radiation is also a good radiator, and in just the same proportion.

The emissivity  $e$  of a nonblackbody is the ratio of the radiant intensity of the body to the radiant intensity of a blackbody source at the same temperature. The reflectivity of a nonblackbody is the ratio of the incident and the reflected radiant intensities. The sum of the emissivity and the reflectivity is unity. Blackbody radiation is observable through a small opening in an opaque enclosure which is all at a uniform temperature. It is approximated by the radiation from deep cavities in a uniformly heated body and in furnaces which are close to thermal equilibrium. Exposed surfaces are never black, and, when their temperatures are measured with an optical pyrometer, the result differs from the true temperature, since it is too low if the surface is in the open and too high if it is in a furnace, the walls of which are hotter than the surface. The spectral emissivities of many materials are known for  $\lambda = 0.65$  micron; and it is possible by the use of available tables to apply corrections to the measured values to determine the true temperature. The values of emissivity vary from about 0.1 for polished copper or gold or 0.3 for polished platinum to 0.8 for oxidized carbon steel or 0.96 for titanium carbide. At a measured temperature of  $1000^{\circ}\text{C.}$ , the true temperature, if  $e$  is 0.1, is  $1196^{\circ}\text{C.}$ , while for  $e = 0.9$  the true temperature is  $1008^{\circ}\text{C.}$ , if the measured surface is in the open.

The correction tables are based on the assumption that the emissivity of the surface is the same at all wave lengths, in which case the nonblackbody is called a gray body and the measurement of radiation at wavelength  $\lambda$  is a true measure of the tem-

perature of the body. Some bodies are selective radiators, that is, they emit radiation which is not in accordance with the blackbody distribution curve. The light from fluorescent lamps, mercury vapor lamps, and from most flames are examples. An optical pyrometer does not measure the temperature of such a source.

**Errors Due to Reflection.** Nonblackbodies are reflectors of radiation. The optical pyrometer measurement is based only on emitted radiation. If an optical pyrometer is sighted on a sheet of white paper in a well-lighted room, a disappearance of filament may be secured giving a temperature reading of perhaps 1000°C. while the paper is at room temperature. This means that the brightness of the reflected red light is as great as that which would be emitted by a blackbody at 1000°C. Any light from a lamp, window, or other source which is reflected from the surface being measured into the pyrometer telescope introduces an error in the reading, and is to be avoided.

Clean surfaces of molten metals are good reflectors and consequently have low emissivity. The emissivity of molten steel at  $\lambda = 0.65$  micron is usually assumed to be 0.4. Particles of slag or of iron oxide floating on the metal have higher emissivities and therefore appear as bright spots on the surface; they are "blacker" than the steel. The correction for an emissivity of 0.4 is applicable to the steel, and it is the darker, clean surface against which the filament should be matched.

An incandescent steel billet usually has a mottled appearance due to scale more or less closely attached to its surface. The scale appears darker than the clean steel surface because it is actually at a lower temperature. In this case the bright spots should be sighted on and a correction corresponding to about 0.8 emissivity applied.

**Calibration.** Optical pyrometers for use in laboratory or plant measurements are calibrated by a substitution method. A standard optical pyrometer which has been calibrated at fixed freezing points is used to measure the apparent temperature of a flat filament of tungsten. A pyrometer to be calibrated is then substituted for the standard and the current at which disappearance is secured is observed. The tungsten filament is not "black," but if the red glass filters in the two instruments are similar, the emissivity corrections are the same for both and a blackbody calibration of the instrument under test will be obtained.

**Sources of Error.** In addition to extraneous light, other sources of error to be avoided are: smoke or fumes between the pyrometer and the source; dust or other deposits on lenses, screens, or lamps; and depleted filament batteries. The pyrometer should be checked from time to time against a standard pyrometer.

A concave portion of an incandescent surface usually appears brighter and therefore hotter than a convex portion of the same surface, that is, it has a higher effective emissivity. Blackbody conditions and true temperature may be closely approximated by sighting into a hole in a hot body, the temperature of which is to be measured.

### Radiation Pyrometry

The Stefan-Boltzmann law states that the radiant energy emitted by a blackbody per unit area in unit time is proportional to the fourth power of its absolute temperature:

$$W = \sigma T^4$$

where  $W$  is the radiant flux per unit area,  $\sigma$  is the Stefan-Boltzmann constant, and  $T$  is the absolute temperature in degrees K.

If the radiating body of area  $A$  is in an enclosure which is at a temperature  $T_0$ , its net loss of energy per second by radiation is given by:

$$U = \sigma A (T^4 - T_0^4)$$

A gray body emits less than a blackbody at the same temperature. For a gray body:

$$U = e, \sigma A (T^4 - T_0^4)$$

where  $e$ , is the total emissivity of the gray body. The experimentally determined value of  $\sigma$  is  $5.6699 \times 10^{-12}$  watt/(cm.<sup>2</sup>)(deg.<sup>4</sup>).

The above facts form the basis for radiation pyrometry as distinguished from optical pyrometry. The term "total radiation pyrometry" would apply to the ideal case, but actually no practical radiation pyrometer can detect all the energy radiated to it by the source. A radiation pyrometer receives the energy radiated from a definite area of the source and focuses it on an absorbing area, the receiver. There it may produce a photoelectric current, if the receiver is a photocell, but more commonly it heats the receiver, increasing its temperature until its rate of loss of heat by conduction, convection, and radiation is equal to the rate at which it is absorbing heat from the radiating source. The rise in temperature may be measured thermoelectrically, by change in resistance of the receiver, by its expansion, making use of a bimetallic spiral, or by changes of pressure in a capsule of gas, to mention only a few of the means that have been used. We shall consider first the thermoelectric method.

The thermocouple or thermopile indicates the rise in temperature of the receiver above its surroundings, and it is unnecessary to maintain a constant reference junction temperature to measure  $t_2 - t_1$ , where  $t_2$  is the temperature of the heated receiver and  $t_1$  is that of its surroundings. This difference usually amounts to only a few degrees, and the rate of loss of heat closely follows Newton's law of cooling, that is, the rate of loss of heat is proportional to  $t_2 - t_1$ . At equilibrium, the rate of loss of heat is equal to the rate of absorption:

$$K(t_2 - t_1) = T_2^4 - T_1^4$$

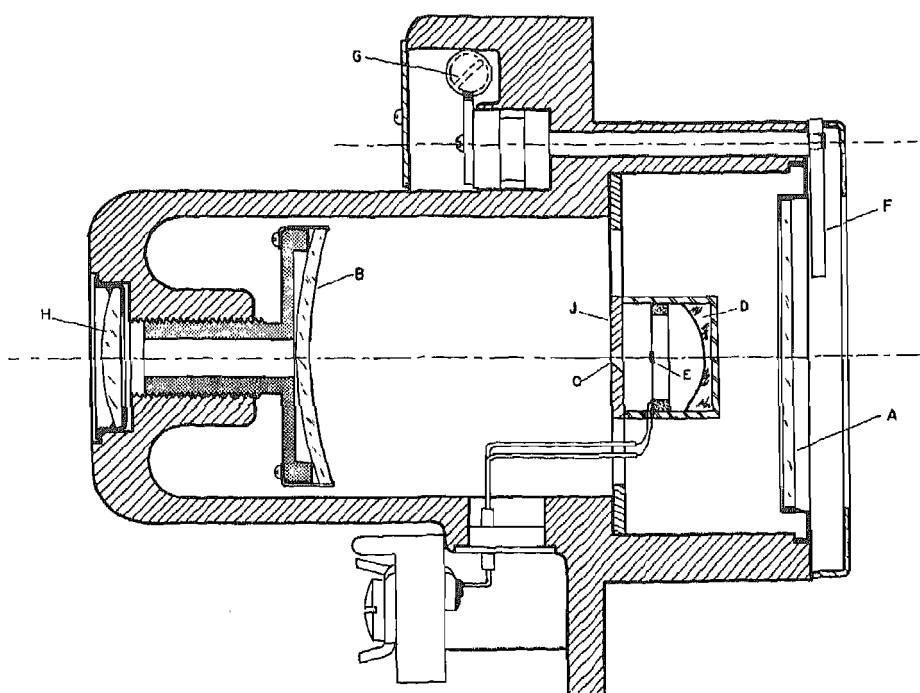
where  $T_2$  and  $T_1$  are the absolute temperatures of the source and of the pyrometer housing respectively. If the e.m.f.  $E$  generated by the thermopile and its rate of loss of heat were both exactly proportional to  $t_2 - t_1$  and if all the radiation from the source which, by the geometrical optics of the system, should heat the receiver actually did so, it would be possible to measure  $E$  at one value of  $T_2$  and by the application of the Stefan-Boltzmann law, to compute the value of  $T_2$  corresponding to any other value of  $E$ . This would be the case with a strictly total radiation pyrometer.

In actual practice,  $E$  is not exactly proportional to  $t_2 - t_1$  for any available thermocouple. Newton's law is departed from because the thermal conductivity of the wires supporting the receiver, and of the air surrounding them, depends on the ambient temperature. The radiation which heats the receiver is not "black," because radiation is absorbed selectively by lenses, windows, mirror surfaces, and the receiver itself. Consequently it is necessary to measure  $E$  at various known temperatures of the blackbody source in order to establish an empirical relationship between  $E$  and  $T_2$  for the particular type of pyrometer, to enable its use for measuring temperatures.

The radiation pyrometer is not in the same category as the standard platinum thermocouple or the disappearing-filament optical pyrometer as a temperature standard. It is essentially an industrial instrument, comparable with the base metal

thermocouples, but covering the whole pyrometric range, with no theoretical upper limit.

**Structure of Radiation Pyrometers.** Radiation pyrometers for industrial use making use of a thermoelectric sensitive element were first introduced about 1902, and since that time they have been produced in many different forms. The focusing means may be either a lens or a concave mirror; the instrument may be either "fixed focus" or adjustable in focus, the sensitive element may be either a single thermocouple, in air or in an evacuated bulb, or a multiple junction thermopile in air. The e.m.f. may be measured with a millivoltmeter or with a potentiometer, either indicating; indicating and recording; or indicating, recording, and controlling.



*Courtesy Leeds & Northrup Co.*

**Fig. 9. Radiation pyrometer.**

The concave mirror is preferred as a means of focusing for two reasons: (1) The image of the source is equally well focused on the receiver for all wave lengths, since the mirror produces no chromatic aberration, while for the lens the image can be sharp for only one wave length, so that the "mean" image is diffuse, and the area of the source contributing to the measurement is poorly defined. (2) Lenses of glass or of vitreous silica absorb completely a considerable part of the long wave length radiation. The radiation reflected by a mirror differs only slightly in mean wave length from that incident on it.

Figure 9 shows schematically the optical features of a modern mirror-type radiation pyrometer. Radiation from a source enters through a thin vitreous silica window A, is reflected by the spherical mirror B, and is brought to a focus on the diaphragm J,

in the center of which there is an aperture *C*. Radiation passing through *C* is reflected by the spherical mirror *D* to the receiver *E* where an image of *C* is formed. The surface of *J* is whitened slightly with magnesium oxide to make it reflect diffusely enough light to make the image of the source visible when viewed through a lens *H* placed behind *B*. The instrument is oriented by the observer so that the image of the portion of the source to be sighted on covers the aperture *C*. Since *B* produces no chromatic aberration and very little spherical aberration, the image of the source, placed at the distance for which the mirror is focused, is very sharp and a very definite portion of the image can be made to cover *C*. The ratio of source distance to requisite source diameter (distance factor) is about 24 to 1 for distances greater than 24 in. At 24 in., the source diameter must be at least 1 in., at 48 in., 2 in., etc. For shorter source distances the distance factor is larger. For distances greater than 20 in., the instrument can be used as a "universal focus" device if properly focused and calibrated for a distance of 24 in.

An adjustable shutter *F* in front of the window *A* serves to regulate the size of the opening admitting radiation so as to adjust the e.m.f. output of the thermopile to match closely an established temperature vs. e.m.f. chart. Fixed entrance diaphragms provide for adjustment of the range of the pyrometer through wide limits. The upper end of the range may be as low as 1000°C. or as high as 1800°C., or even higher if needed, for a maximum e.m.f. output of 20 millivolts. The scale is nonlinear, following approximately the fourth power law for the relationship between temperature and e.m.f. Since the low end of the range is thus compressed, e.m.f.'s lower than 1 millivolt on a 20-millivolt range are not useful in measuring temperature. The range terminating at 1000°C. starts at 450°C. and that terminating at 1800°C. starts at 825°C. In the upper half of the range, changes of source temperature of the order of 0.1% of the measured value are easily detected.

The time required to reach equilibrium after a sudden large change in temperature of the source is dependent on the heat capacity of the receiver and the rate at which it dissipates heat. This time of response for the instrument described is from 1 to 10 seconds, depending on size of receiver.

**Emissivity.** The uncertainties of measurement due to nonblackbody conditions are even more serious in the case of the radiation than in that of the optical pyrometer. The errors are larger and the values of total emissivity  $\epsilon_t$  are in general not very well known, and do not apply exactly to any practical radiation pyrometer. Accuracy is attainable only when blackbody radiation is measured. This is assured in practice only when the source is a uniformly heated enclosure. A deep closed-end tube inserted in the region where the temperature is to be measured approaches this requirement closely, and offers a valuable means of measuring temperatures in surroundings where any thermocouple would be liable to contamination or destruction. In almost any other condition, emissivity must be taken into account in interpreting readings with a radiation pyrometer in terms of true temperature.

**Photoelectric Pyrometers.** The radiation emitted by a hot body can also be detected and evaluated in terms of temperature of source with the aid of photoelectric cells (*q.v.*). There are three varieties of photocells which have been used for this purpose.

(1) The emission-type cell, in which the radiation, falling on a photosensitive metal surface in an evacuated or gas-filled bulb, causes it to emit electrons. A voltage of the order of 100 volts applied between the sensitive plate and an anode produces



a current through the cell, the strength of which depends upon the quantity and wave length of the incident radiation. The current flow can be evaluated by calibration at known source temperatures, so as to serve as a measure of source temperature.

(2) The barrier-layer-type cell, in which the incident radiation generates an e.m.f. between two electrodes separated by a sensitive layer of selenium or of copper oxide. The current produced by this e.m.f. in a low-resistance external circuit serves as a measure of the temperature of the source, when an image of a definite area of the source is formed on the sensitive surface.

(3) The photoconductive-type cell (lead sulfide cell) in which incident radiation increases the electrical conductivity of a light-sensitive film of a material such as lead sulfide. The resistance of this film serves as a measure of the temperature of the source.

Photocells (1) and (2) have very little sensitivity for wave lengths more than 1 micron and therefore are not adapted for measurement of temperature below 1000°C. Because of the narrowness of the band of wave lengths to which they are sensitive, their output increases much more rapidly with increase in absolute temperature than for the thermoelectric-sensitive elements. It is roughly proportional to the 13th power of the absolute temperature of the source. Consequently a drift of sensitivity of the photocell of 10% affects the temperature reading by less than 1%. The temperature-scale graduations widen rapidly toward the upper end of the scale. Response to change in temperature is practically instantaneous.

Because of the high-power law, the emissivity corrections to be applied to gray body readings are smaller than in the case of the thermoelectric sensitive elements.

The lead sulfide cell (3) has a considerable sensitivity at longer wave lengths, making it available for measurements of temperature down to 120°C., when lenses and windows having high transmission in the infrared are used. The cell is relatively unstable and for good precision a null type method of measurement is used in which the cell is exposed alternately to radiation from the unknown and a known source, producing pulsations in the current except when the radiations from the two sources are equal. The pulsations are amplified electronically, and reduced to zero by adjustment of the intensity of the known sources.

**Uses.** The radiation pyrometer is to be recommended in place of a thermocouple in the following cases: (1) where a thermocouple would be poisoned by furnace atmospheres; (2) for measurement of surface temperatures; (3) for measurement of the temperature of moving objects; (4) for measurement of temperatures beyond the range of base metal thermocouples; (5) where mechanical conditions, such as vibration or shock, make a hot thermocouple short-lived; and (6) where high speed of response to temperature changes is required.

It replaces the optical pyrometer where it is desired to record and control temperatures above 1600°C. It is requisite to this substitution that the source be large enough to fill the field of the radiation pyrometer.

### Color Temperature

It is a familiar fact that the color of an incandescent body, such as the filament of a tungsten lamp, is dependent on its temperature. As it is heated, the filament is first black, then dull red, bright red, yellow, and finally "white." There is a characteristic color for each temperature. The filament is a gray body and therefore it is less bright than a blackbody at the same temperature, but its color is the same as that of

the blackbody, since by definition of a gray body its spectral distribution is the same as that of a blackbody at the same temperature. Hence when color is used as a basis of measurement, no emissivity corrections are involved. Instruments have been devised, such as the Naeser color pyrometer and the Biopix pyrometer which make use of this principle.

Another method of approach is to measure the ratio of intensity of radiation at two different wave lengths, such as red and green. For either a gray or a blackbody, this ratio is the same function of the temperature, and can be used as a measure of temperature, independent of emissivity. Photoelectric-sensitive elements are used in this measurement.

The open-hearth melter, wearing goggles of cobalt blue glass which has transmission bands, one in the blue and the other in the red, unconsciously uses a variation of this method. Because of the variation in ratio, the purple sensation changes rapidly with temperature. With experience he is able to estimate temperature around 3000°F. within from 30 to 75 deg. F.

These color temperatures are not to be confused with the film colors on an iron surface which the blacksmith of former days used to determine when to quench a red-hot tool to secure the desired temper.

### Miscellaneous Methods

**Melting-Points as Measures of Temperature.** This method of indicating that a certain temperature has been reached consists in applying a mark, a wash, or a pellet to the body to be heated. Melting of this application takes place at some definite temperature and is detected by observing the change from a rough to a glossy surface. Under the trade-marked name Tempilstick these materials are supplied as a series of compounds ranging in melting point from 113 to 2500°F. at intervals from 12.5 to 50 deg. F. They are said to have a mean accuracy of  $\pm 1.0\%$  of the stated temperatures. Their use involves no instrumentation and no special training of the operator. A series of marks with crayons of different melting points can serve, on subsequent examination, to indicate the highest temperature attained by the work-piece.

**Pyrometric Cones.** See Vol. 3, pp. 589, 590.

### Choice of Method

There is a wide choice open to the person who wishes to measure temperatures. The simplicity of expansion thermometers and their inexpensiveness make their use almost obligatory in many cases. In the range of temperatures from about  $-183$  to  $+450^{\circ}\text{C.}$  where high precision is not required, liquid-in-glass thermometers are indispensable. If the location where temperatures in this range are to be measured is unfavorable to the installation and reading of a mercury thermometer or if it is required that temperatures be recorded or controlled, consideration must be given to pressure-type thermometers, resistance thermometers, and thermocouples. If the recorder can be located within a few feet of the sensitive element, the gas- or vapor-pressure-type instrument are usually adequate and less costly, though inferior in precision to resistance thermometers and thermocouples. Replacement of sensitive elements is a more difficult operation for the pressure-type instruments than for the electrical. In its accepted range, the resistance thermometer has advantages over the thermocouple in sensitivity and precision, and in operation, if desired, from an a.c.

supply, thus eliminating all need for dry cells, standard cells, current standardization, and reference junction compensation. The thermocouple can be inserted in locations inaccessible to resistance thermometers, has a higher speed of response, and is less costly. Resistance thermometers and thermocouples are definitely competitive over the range from  $-200$  to  $+500^{\circ}\text{C}$ . For recording and controlling above  $500^{\circ}\text{C}$ . the thermocouple and the radiation pyrometers are competitive up to about  $1600^{\circ}\text{C}$ ., where the thermocouple drops out. The optical pyrometer is the most precise means of measuring temperatures above  $1063^{\circ}\text{C}$ ., but it cannot be used to operate recorders and controllers.

### Bibliography

- (1) A.S.M.E. Power Test Codes, *Instruments and Apparatus*, Part 3, "Temperature Measurement": ch. 1, General (1931); ch. 2, Radiation Pyrometers (1935); ch. 3, Thermocouple Thermometers or Pyrometers (1940); ch. 4, Resistance Thermometers (1945); ch. 5, Pyrometric Cones (1931); ch. 6, Liquid-in-Glass Thermometers (1931); ch. 7, Bourdon Tube Thermometers (1931); ch. 8, Optical Pyrometers (1933).
- (2) Baker, H. D., Ryder, E. A., and Baker, N. H., *Temperature Measurement in Engineering*, Vol. I, Wiley, N.Y., 1953.
- (3) British Standard Code, Temperature Measurement, B.S. 1041 (1943).
- (4) Burgess, G. K., and Le Chatelier, H., *The Measurement of High Temperatures*, Wiley, N.Y., 1911.
- (5) Dike, P. H., Temperature Measurements with Rayotubes, Tech. Pub. EN-33B(1), Leeds & Northrup Company, Philadelphia, 1953.
- (6) Dike, P. H., Thermoelectric Thermometry, Tech. Pub. EN-33A(1), Leeds & Northrup Company, Philadelphia, 1954.
- (7) Foote, P. D., Fairchild, C. O., and Harrison, T. R., "Pyrometric Practice," *Natl. Bur. Standards (U.S.), Technol. Paper*, No. 170 (1921).
- (8) *Natl. Bur. Standards (U.S.), Circ.*, 508 (1951).
- (9) *Natl. Bur. Standards (U.S.), Research Paper*, 2415 (1953).
- (10) Rhodes, J. T., *Industrial Instruments for Measurement and Control*, McGraw-Hill, N.Y., 1941.
- (11) Ribaud, G., *Pyrometrie Optique*, editions de la revue d'optique theoretique et instrumentale, Paris, 1931.
- (12) Sesman, R. B., *Pyrometry of Solids and Surfaces*, Am. Soc. Metals, 1940.
- (13) Symposium Committee of the Am. Inst. Physics, Natl. Bur. Standards, Natl. Research Council, *Temperature: Its Measurement and Control in Science and Industry*, Reinhold, N.Y., 1941.
- (14) "Symposium on Pyrometry," *Trans. Am. Inst. Mining Met. Engrs.*, 62 (1920).
- (15) Weber, R. L., *Temperature Measurement and Control*, Blakiston, Philadelphia, 1941.
- (16) Weber, R. L., *Heat and Temperature Measurement*, Prentice-Hall, N.Y., 1950.
- (17) Wood, W. P., and Cork, J. M., *Pyrometry*, McGraw-Hill, N.Y., 1941.

P. H. DIKE

**TEMPERING OILS.** See *Petroleum (products)*, Vol. 10, p. 170.

**TEPHROITE**,  $\text{Mn}_2\text{SiO}_4$ . See *Silica and silicates (mineral)*, Vol. 12, pp. 279, 280.

**TERBIUM**, Tb. See *Rare-earth metals*.

**TEREBENE.** See *Emetics and expectorants*, Vol. 5, p. 684.

**TEREPHTHALIC ACID**,  $p\text{-C}_6\text{H}_4(\text{COOH})_2$ . See *Phthalic acids*, Vol. 10, p. 600.

**TERNE PLATE.** See *Lead alloys*, Vol. 8, p. 262; *Tin and tin alloys*.

## TERPENE RESINS

Pale amber, transparent, thermoplastic polyterpene hydrocarbon resins, of the type formula  $(C_{10}H_{16})_n$ , have been produced and sold on a commercial scale since 1938. These resins are characterized by ring-and-ball softening points (S.P.) ranging up to about 135°C.; they are soluble in a great variety of organic solvents, including hydrocarbon solvents, and are of good color stability. They are used, in conjunction with other materials, in the formulation of a wide variety of end products, including adhesives, adhesive tapes, rubber goods, and coating compositions. Depending on the nature of the end use, the terpene resins are supplied either in solid form or in solution in hydrocarbon solvents; the solid forms are made in a wide range of softening points or molecular weights.

These polyterpene resins are derived primarily from the catalytic polymerization, in solution, of the bicyclic monoterpene pinene,  $C_{10}H_{16}$ , principally the  $\beta$ -isomer (no-pinene), and may be regarded as essentially polymers from  $\beta$ -pinene. The pinene in turn is derived from gum and sulfate turpentine, from both of which it is recovered by fractional distillation. See *Terpenes (mono-, cyclic)*.

This article is concerned only with these hydrocarbon resins, and does not cover other terpene-derived resinous substances, such as rosins (*q.v.*) and the terpene-phenol resins. The latter are produced by reacting terpene hydrocarbons or alcohols with phenol in the presence of acid catalysts, followed by catalytic resinification of the resulting substituted phenol with a reactive substance such as formaldehyde (1,6). Such terpene-modified phenolic resins exhibit among other properties increased solubility in drying oils. They are useful in adhesives and in various types of coatings, including particularly wax emulsions, varnishes, paints, and heat-setting printing inks. Certain resins are also antioxidants for rubber.

## Physical Properties

The commercially available polyterpene resins are produced with a variety of softening points (measured by the A.S.T.M. ring-and-ball method E28-51T), ranging from +10 to +135°C., corresponding to a range from viscous liquid to hard, brittle solid polymers at ordinary temperatures. The average molecular weights of these polymers increase as the softening points increase. A molecular weight of about 1200 to 1250, measured cryoscopically in benzene, is characteristic for a polymer of 125 to 135°C. softening point. In common with polymers generally, the polyterpenes are mixtures of polymers of various molecular weights and chain lengths. A characteristic molecular-weight distribution obtained by fractionation for a commercial 135°C. softening-point polyterpene resin is shown in Table I. The fractionation was accomplished by partial precipitation from amyl alcohol, the general procedure involving solution of the resin in hot amyl alcohol, followed by cooling, decanting the amyl alcohol solution from the precipitated higher-molecular-weight polymers, and steam distillation of the decanted solution to remove the alcohol. Fractions 1-6 were so obtained, increasing amounts of amyl alcohol being required for the successive fractions because of the decreased solubility associated with increased molecular weight.

These polymers are typically thermoplastic, and merely soften or harden as they are heated or cooled, no irreversible change occurring as long as the heating temperature is kept below that at which pyrolytic reactions set in. In common with other

TABLE I.

Fraction	Weight % of original resin	Molecular weight (cryoscopic in benzene)
1	12.8	750
2	16.9	830
3	11.5	910
4	12.8	1150
5	12.9	1620
6	16.9	1910
7	16.2	3540

amorphous hydrocarbon resins, these polymers show no sharply defined liquefaction or solidification temperatures, and their softening points are therefore measured by arbitrary standard test methods.

The polymers are slightly less dense than water, resulting in a relatively high bulking value compared to other polymeric materials. Values for the specific gravity of these resins range between about 0.97 and 1.00, depending on the softening point or molecular weight, the exact composition of the monomeric terpene mixture polymerized, and the method of production.

The resins exhibit solubility in, or compatibility with, a wide range of materials. Complete miscibility exists with liquid paraffinic, naphthenic, and aromatic hydrocarbons, chlorinated hydrocarbons, higher alcohols, higher ketones, esters, and drying oils. Compatibility is exhibited with rosin, ester gum, waxes, including paraffin wax, polyisobutylenes, petroleum residues and pitches, mineral oils, and certain types of petroleum hydrocarbon polymers. Under appropriate conditions, compatibility is exhibited with rubber and modified rubbers, including synthetic rubbers such as GR-S. Compatibility with cellulose ethers and esters is, however, quite limited.

Inasmuch as these resins are entirely hydrocarbon in nature they are moisture resistant and possess good dielectric properties.

### Chemical Properties

As essentially pinene polymers, principally polymers from  $\beta$ -pinene, the terpene resins exhibit properties typical of polymeric hydrocarbons including chemical inertness. They are inert to dilute mineral acids, alkalies, and salt solutions, and are characterized by acid numbers and saponification numbers less than four and approaching zero. Similarly they are resistant to heat over a wide range of temperatures, varying only in fluidity with temperature.

The detailed chemical structure of the terpene resins cannot be regarded as satisfactorily elucidated. Published data in the chemical literature and patented art have indicated these polymers to be susceptible to both halogenation and catalytic hydrogenation, and to reaction with ozone to give polymeric ozonides (5,7,9). For example, the reported weight of hydrogen absorbed by a catalytic polymer made from  $\beta$ -pinene was 1.2%. This is equivalent to 0.82 mole of hydrogen per  $C_{10}H_{16}$  recurring unit in the polymer chain. Based in part on these considerations, and in part on physical properties, Roberts and Day (5) speculated that the catalytic polymerization of  $\beta$ -pinene involved more than a simple chain addition reaction of monomer molecules and that isomerization occurred during the polymerization to give a polymer comprising a chain of recurring monocyclic  $C_{10}H_{16}$  terpene units each containing a carbon-

carbon double bond. Powers (4) has also suggested the recurring unit of polymers from pinene to be monocyclic and unsaturated, proposing a formula different in detail and in point of linkage.

More recent studies of these polymers by infrared spectrophotometric techniques have indicated that the polymers contain notably less unsaturation than would be required for a chain of recurring monocyclic terpene units but more than would be the case for a simple addition polymerization of  $\beta$ -pinene molecules yielding a polymolecule containing only a single terminal double bond (3). Part, but not all, of the unsaturation observed by infrared examination appears to represent terminal double bonds in the polymolecules, inasmuch as it decreases with increasing molecular weight.

These observations imply that the pinene polymerization is, as postulated by Roberts and Day, more complex than simple addition, but that the final recurring unit structure is not solely monocyclic. Pending further elucidation it seems preferable to avoid the term poly- $\beta$ -pinene, insofar as the latter may imply simple addition polymerization.

### Manufacture

Basically, terpene hydrocarbon resins are produced by the controlled treatment of the monomer in solution in a hydrocarbon diluent with a catalyst of the Friedel-Crafts type, such as anhydrous aluminum chloride. The polymerization reaction is highly exothermic, and provision is made for adequate agitation and heat exchange. On the completion of the reaction the mixture is freed of catalyst, and the catalyst-free polymer solution is distilled with steam at reduced pressures to remove solvent, any unreacted terpenes, and also any steam-volatile low-terpene polymers. The residual nonvolatile molten resin may then be poured into drums to cool, or used for the preparation of terpene resin solutions.

Of the two naturally occurring isomers of pinene, the  $\beta$ -form is greatly superior to the  $\alpha$ -isomer in catalytic polymerization, with respect to polymer yield and polymer molecular weight or softening point, and it was this finding which laid the basis for the economical commercial production of terpene resins (8). Both  $\alpha$ - and  $\beta$ -pinene occur in gum turpentine and in many crude sulfate turpentines.  $\beta$ -Pinene is virtually nonexistent in steam-distilled wood turpentine. In the case of gum spirits of turpentine from longleaf pine, a typical composition is 63%  $\alpha$ -pinene, 33%  $\beta$ -pinene, and 4% higher-boiling constituents (2). Moderate variations in these percentages occur with variation in the source, but the  $\beta$ -pinene content is seldom below 29%. In contrast, sulfate turpentines may vary very widely in composition, depending on the geographical area, source, and processing techniques involved. Usually the pinenes are accompanied by smaller quantities of higher-boiling monocyclic terpenes, particularly dipentene (or limonene). See also *Terpenes (mono-, cyclic)*; *Turpentine*.

For appropriate use as charge material for polymerization to terpene resins, it is advantageous to separate by fractionation the bulk of the  $\alpha$ -pinene from the original turpentine, and to prepare a relatively concentrated fraction of  $\beta$ -pinene. Such processing not only yields highly concentrated  $\beta$ -pinene of particular usefulness for making terpene resins, but also gives highly concentrated  $\alpha$ -pinene fractions which are themselves useful in other chemical processes, particularly the manufacture of synthetic camphor.

The boiling points of the isomeric pinenes, and also of dipentene, are sufficiently close that relatively efficient fractionation is required for this purpose. These boiling points at atmospheric pressure are:  $\alpha$ -pinene 156°C.,  $\beta$ -pinene 165°C., and dipentene 176.5°C.

Depending on the efficiency of fractionation, commercial  $\beta$ -pinene will usually contain, as the principal other constituents,  $\alpha$ -pinene and dipentene. Inasmuch as these are all  $C_{10}H_{16}$  terpene isomers, the empirical formula of the final polymer,  $(C_{10}H_{16})_n$ , is not affected.

For effecting the polymerization reaction, the  $\beta$ -pinene fraction is diluted with a refined hydrocarbon solvent, such as a naphtha cut. This dilution prevents the viscosity of the reaction mixture from becoming excessive as the polymerization reaction proceeds, thus facilitating agitation, circulation, heat exchange, and final catalyst removal. In practice, dilution of the pinene to a concentration between about 40 and 50% is satisfactory.

The conditions during polymerization are very closely controlled. In batch reaction it is necessary to add the Friedel-Crafts catalyst carefully and gradually because of the vigorously exothermic nature of the reaction. By careful control and instrumentation, temperatures are maintained within a few tenths of a degree, the reaction heat being removed by heat exchange with cold water or brine. Temperatures of polymerization are moderate, practical operations generally being within the range 20–50°C.

Usually, after heat evolution from the reactions has subsided, an additional contacting period with the catalyst is provided to insure essentially complete conversion of the monomers to polymer.

Before recovery of the resin itself, complete removal of the halide catalyst is necessary. This may be effected by successive washing with water and dilute aqueous alkali, followed by separation of the aqueous material from the hydrocarbon phase. Removal of the catalyst changes the reaction mixture from its original dark red color to a pale yellow. Special subsequent treating steps are used to remove final traces of halogen.

The catalyst-free, neutral resin solution is then charged to batch distillation kettles. At elevated temperatures, volatile oils are distilled out, final operating conditions of steam and vacuum being used to remove any more difficultly volatile, heavy, polymeric oils produced in the reaction. The recovered diluent naphtha may be recycled in subsequent charges to the polymerizer.

At the elevated stillpot temperatures (above 200°C.) used in the finishing step, the final resin, free of diluent, unreacted terpenes, and steam-volatile heavy oils, is present as a viscous, pale amber liquid ready for transfer. Depending on the use to which the resin is to be put, the molten resin may be poured directly into drums, which are then allowed to cool before shipment, or it may be transferred to a separate vessel to make terpene resin solution. The resin solutions normally contain 45 or 65% solids in mineral spirits.

The different grades of commercial terpene resins, sold under the trade name Piccolyte, are produced by appropriate choice of conditions in the manufacturing step. These grades range from 10°C. S.P. to 135°C. S.P., the lower-softening point products being viscous liquids at ordinary temperature. For shipment, these soft or plastic grades are poured into heavy drums of the open-head type; the solid grades are poured into light-gage drums.

For certain specialty uses where a water-white terpene resin is required, the regular, pale amber product is catalytically hydrogenated in solution, to reduce the unsaturation and color, and to permit the recovery, on redistillation of the solvent, of an essentially colorless resin product.

**Economic Aspects.** The terpene resins have taken their place in a number of specialty uses industrially, for many of which no other resin has been found to possess equally satisfactory characteristics. Although their production is limited in comparison with many other polymeric products, such as phenolics and molding resins, such production has increased substantially since their initial manufacture in the late 1930's by the Pennsylvania Industrial Chemical Corporation.

Their manufacture from raw materials derived from turpentine represents a chemical utilization of a naturally occurring product, and is to that extent helpful in stabilizing turpentine operations and marketing. They provide a use for  $\beta$ -pinene, whereas other chemical uses of terpene hydrocarbons from turpentine are largely based on  $\alpha$ -pinene as a raw material.

Inasmuch as  $\beta$ -pinene fractions are recoverable from both gum spirits of turpentine and from many crude sulfate turpentines, the production of terpene resins is connected with both the naval stores and pulping industries, and the magnitude of production is controlled in part by the magnitude of gum spirits and pulping operations.

In July 1954, the selling price of the resins ranged between \$0.185 and \$0.200 per pound depending on quantity and on the softening-point grade.

### Uses

The field of usefulness for terpene resins is based especially on the combination of solubility, light color, stability, and chemical inertness, as well as their lack of toxicity. Particularly important to the use pattern for terpene resins are the very definite and desirable adhesive properties imparted to formulations involving natural or synthetic rubbers. They are usually used in conjunction with other materials in various industrial formulations.

The wide application of the resins in adhesives and in the preparation of adhesive tapes includes their use in rubber cements, friction tapes, and with polyisobutylene. Another wide field of application is in rubber goods, including toys, hose and mechanical rubber goods. The resins are also useful in paints and varnishes, concrete curing, chewing gum, paper coatings, and leather goods, as well as in laminating and polish waxes, and in inks. The compatibility between terpene resins and natural and synthetic rubbers is of particular importance, since a number of these uses are based on formulations involving such mixtures.

### Bibliography

- (1) Mattiello, J. J., *Protective and Decorative Coatings*, Wiley, N.Y., 1941, p. 568.
- (2) Palkin, S., *U.S. Dept. Agr., Tech. Bull.*, No. 276, (1932)
- (3) Pennsylvania Industrial Chemical Corp., Research Laboratory, unpublished data.
- (4) Powers, P. O., *Synthetic Resins and Rubbers*, Wiley, N.Y., 1943, p. 173.
- (5) Roberts, W. J., and Day, A. R., *J. Am. Chem. Soc.*, **72**, 1226 (1950).
- (6) Turkington, V. H., and Allen, I., Jr., *Ind. Eng. Chem.*, **33**, 966 (1941).
- (7) U.S. Pat. 1,939,932 (Dec. 19, 1933), C. A. Thomas (to Dayton Synthetic Chemicals).
- (8) U.S. Pat. 2,335,912 (Dec. 7, 1943), S. G. Burroughs (to Pennsylvania Industrial Chemical Corp.).
- (9) U.S. Pat. 2,405,558 (Aug. 13, 1946), J. N. Borglin (to Hercules Powder Co.).

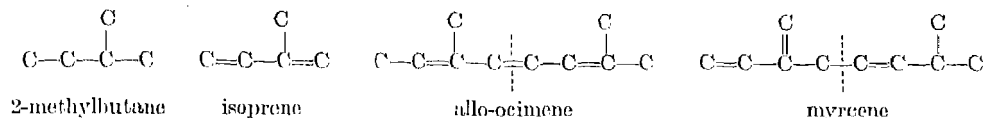
W. J. ROBERTS AND A. L. WARD



## TERPENES AND TERPENOIDS

Monoterpenoids—acyclic.....	p. 708	Diterpenoids.....	p. 752
Monoterpenoids—cyclic.....	720	Triterpenoids.....	760
Sesquiterpenoids.....	740		

The terpenes embrace a vast family of chemical compounds which are isolated chiefly from essential oils and resins of plants (see *Oils, essential*; *Resins, natural*). Strictly speaking, they are acyclic and cyclic hydrocarbons whose molecular formulas are some multiple of  $C_5H_8$ . Usually this definition is expanded to include naturally occurring and synthetic alcohols, aldehydes, ketones, and other derivatives having the same carbon skeleton as the parent terpene hydrocarbon and more properly called *terpenoids* (a term also used to include the terpenes proper). A characteristic feature of these hydrocarbons and their derivatives is the presence of the 2-methylbutane carbon structure as a recurring unit.



Most of the hydrocarbons (except the tricyclic  $C_{10}H_{16}$  members) are unsaturated, and they can be considered condensation products of isoprene,  $C_5H_8$  (see Vol. 7, p. 605); according to the *isoprene rule* noted by Wallach in 1887, these isoprene units are arranged head-to-tail, though there are some exceptions. The terpenes (and their derivatives) can therefore be classified according to the number of isoprene units—one, two, three, four or more—into hemiterpene (isoprene),  $C_5H_8$ ; monoterpenes,  $C_{10}H_{16}$ ; sesquiterpenes,  $C_{15}H_{24}$ ; diterpenes,  $C_{20}H_{32}$ ; and polyterpenes,  $(C_5H_8)_n$ , of which the most numerous are the  $C_{30}$  triterpenoids. Also included are some closely related compounds such as geraniolene,  $C_9H_{16}$ , and santene,  $C_9H_{14}$ , and their derivatives. The carotenoids ( $C_{40}$ ) (see "Vitamin A" under *Vitamins*), rubber and gutta percha (see Vol. 11, pp. 815, 825) are also isoprenoid compounds.

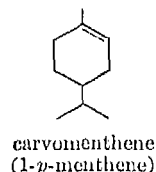
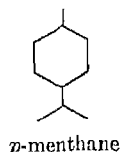
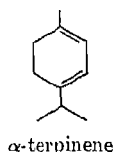
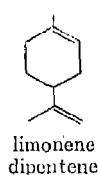
These classes of terpenes may be further subdivided into acyclic, monocyclic, bicyclic, etc. The degree of unsaturation depends upon the number of carbon atoms (number of isoprene units) and the number of rings, one double bond disappearing for each carbon-to-carbon bond formed. Thus in the monoterpenes the number of ethylenic linkages varies from none in the tricyclic hydrocarbons to three in the acyclic. *Isopropenyl-isopropylidene isomerism*, deriving only from the position of the double bond in the head of one of the isoprene units ( $\text{CH}_2=\text{C}(\text{CH}_3)-$  and  $(\text{CH}_3)_2\text{C}=\text{C}-$ ), is typical of many terpenoids (as limonene and  $\alpha$ -terpinene—see the formulas below), and the forms are distinguished only with difficulty particularly among the acyclic monoterpenes and their derivatives. Many other types of structural isomerism exist among the terpenes (see, for example, the formulas for bicyclic and tricyclic monoterpenes below), as well as both types of stereoisomerism, optical and geometrical.

**Nomenclature and Formulas.** The common names of most terpenoids are derived from the botanical origins of the compounds, and the designations  $\alpha$ -,  $\beta$ -,  $\gamma$ -, etc., are used merely to differentiate isomers without positional significance. The structural formulas for ring compounds are usually written without showing carbon or hydrogen atoms, a bond attached to a ring denoting a methyl group and a double bond a methylene group (see below). Even acyclic compounds are frequently written similarly, in partial ring form, particularly to bring out relationships to cyclic compounds. Formulas for polycyclic terpenoids once were always oriented in the opposite way from sterols and steroids (*q.v.*), that is, from the upper left to the lower right, but di- and especially triterpenoid

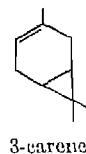
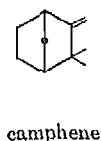
formulas are more and more being oriented and numbered like the steroids as stereochemical relationships are elucidated.

The **monoterpenoids** ( $C_{10}$ ) are subdivided into acyclic, monocyclic, bicyclic, and tricyclic monoterpenoids. The *acyclic* terpenes, of which allo-ocimene and myrcene are examples, are aliphatic hydrocarbons containing three olefinic double bonds.

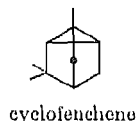
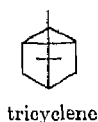
The *monocyclic* terpenes, for example, limonene (or its optically inactive isomer dipentene) and  $\alpha$ -terpinene, contain one six-membered ring. They contain two double bonds, but other compounds such as *p*-menthane and carvomenthene (1-*p*-menthene), having the same carbon skeleton, are included in common usage.



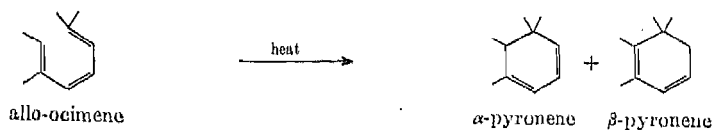
The *bicyclic* terpenes, of which  $\alpha$ -pinene, camphene, and 3-carene are examples, contain two fused rings and one double bond:



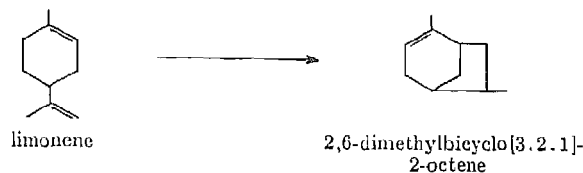
The *tricyclic* terpenes differ from the bicyclic terpenes in having an additional carbon-carbon bond or bridge instead of an olefinic double bond. Tricyclene and cyclofenchene are examples of this class:



These classes of monoterpenes are closely related and one class is frequently prepared from the other. Under acid isomerization conditions, for example,  $\alpha$ -pinene, a bicyclic terpene, forms monocyclic and tricyclic terpenes in addition to isomeric bicyclic terpenes, as in the synthesis of camphene (p. 728). Thermal cracking of  $\alpha$ -pinene forms acyclic and monocyclic terpenes, as in the chief synthesis of allo-ocimene. The conversion of acyclic to monocyclic hydrocarbons and of monocyclic to bicyclic hydrocarbons is less common than the reverse processes (although acyclic alcohols and aldehydes are readily cyclized to unsaturated derivatives of *p*-menthane or of 1,1,3-trimethylcyclohexane; see, for example under "Citral" p. 717). Allo-ocimene is, however, converted to the cyclic pyronenes by thermal cyclization:



Myrcene is similarly converted to camphorene, a monocyclic diterpene (see p. 758). In addition, monocyclics have been converted to bicyclics by acid polymerization:



However, the conversions to pyrenenes and the bicyclooctene are not reversals of the ring-opening processes since the carbon skeletons of the products differ from those of the naturally occurring monocyclic and bicyclic terpenes.

The **sesquiterpenoids** ( $C_{15}$ ) of known constitution exhibit an even greater variety of structure than the monoterpenes, and the structures of many are still unknown. Among those well characterized are *acyclic* alcohols and *monocyclic* hydrocarbons, alcohols, and one quinone, both of these subclasses containing three olefinic linkages; *bicyclic* compounds derived from naphthalene, azulene (cyclopentacycloheptene), and other fused ring systems and containing one or two olefinic linkages; and *tricyclic* hydrocarbons and alcohols containing one olefinic linkage. One ketone, eremophilone (see p. 750), derived from naphthalene and containing two olefinic linkages, is a notable exception to the isoprene rule because of an angular methyl group on a carbon adjacent to another bearing a methyl group. Because of a certain amount of interconversion among the above types of sesquiterpenoids, a division based on the dehydrogenation products (derivatives of naphthalene, azulene, etc.) is considered preferable to one based on the number of rings.

Still less is known about the **diterpenoids** ( $C_{20}$ ) as a whole than about the sesquiterpenoids. However, well-characterized compounds include the *acyclic* alcohol phytol, containing one double bond; the *monocyclic* hydrocarbon camphorene, with four double bonds; and a number of *bicyclic* and *tricyclic* acids, alcohols, and phenols, containing for the most part two double bonds, the best known of these compounds being the tricyclic resin acids of the abietic and pimaric types. As with the sesquiterpenoids, the most satisfactory division is based on dehydrogenation reactions, since the bicyclic compounds after cyclization give the same dehydrogenation products as the tricyclic compounds. These products are retene (7-isopropyl-1-methylphenanthrene), formed by the abietic-type acids; pimanthrene (1,7-dimethylpimanthrene), from the pimaric-type acids; and 1,7,8-trimethylphenanthrene, first obtained from a derivative of agathic acid, a bicyclic resin acid. See also *Rosin*.

Some **triterpenoid** (C<sub>33</sub>) saponins (*q.v.*) have not been well characterized, but the triterpenoids themselves have been and form a very large group. They include two compounds obtained from animal sources: the *acyclic* hydrocarbon squalene (from fish oils) containing six double bonds, and the *tricyclic* alcohol ambrein (from ambergris), containing two double bonds. The *tetracyclic* compounds, principally the alcohols lanosterol and agnosterol (from wool grease) have recently been found to be nonisoprenoid and closely related to sterols (*q.v.*) such as cholesterol. The largest division of the triterpenoids therefore consists of the *pentacyclic* compounds, containing one double bond; this bond is in the middle ring in the  $\beta$ - and  $\alpha$ -amyrin groups and is comparatively inactive, whereas in the lupeol-betulin and taraxasterol groups it is in an isopropenyl group or in the terminal ring (E) and is active. Although these

pentacyclic compounds are isoprenoid, they have also been related stereochemically to the steroids.

**Uses.** Many of the terpenes, principally the monoterpenes, are important articles of commerce and are used directly or are the raw materials for the preparation of perfumes (*q.v.*), flavors (*q.v.*), protective coatings, pharmaceuticals, insecticides, bactericides, flotation agents, condensation catalysts, extreme-pressure lubricant additives, adhesives, solvents, and plasticizers. The importance of terpenes may be judged from the figure of 28,233,500 gal. of turpentine (chiefly bicyclic monoterpenes) produced in the United States during the naval stores year April 1952–March 1953 (see *Turpentine*). Although in the past the major use of terpenes has been as solvents, they are becoming increasingly important for chemical synthesis.

### Bibliography

- (1) Barton, D. H. R., and Harper, S. R. H., in Rodd, *Chemistry of Carbon Compounds*, Elsevier, Houston, Texas, and Amsterdam, 1953, Vol. IIB, Chs. XII–XVI.
- (2) *Elsevier's Encyclopaedia of Organic Chemistry*, 1940–1954, Vols. 12A, 12B, 13, 14 and Supplement.
- (3) Simonsen, J. L., and Owen, L. N., *The Terpenes*, 2nd ed., University Press, Cambridge, England, 1947, 1949, Vols. I and II; Simonsen, J. L., and Barton, D. H. R., 1953, Vol. III.
- (4) *Thorpe's Dictionary of Applied Chemistry*, 4th ed., 1954, Vol. 11, pp. 487–542, 726–737.

W. S. ROPP

### MONOTERPENOIDS—ACYCLIC

This section includes the naturally occurring hydrocarbons, alcohols, aldehydes, ketones, and closely related compounds, including some monocyclic ketones derived from citral, an acyclic aldehyde. A number of the alcohols and aldehydes constitute

TABLE I. Production and Sales of Industrially Important Acyclic Monoterpenoids (1953).

Commodity	Production, 1000 lb.	Sales		
		Quantity, 1000 lb.	Value, \$1000	Unit value per lb.
Citral.....	53	48	139	2.91
Citronellal.....	—	1	1	1.68
Citronellol.....	183	165	250	1.51
Citronellyl acetate.....	—	3	7	2.25
Citronellyl propionate.....	3	3	16	5.23
Geraniol.....	551	521	436	0.84
Geranyl acetate.....	30	27	35	1.32
Geranyl formate.....	2	2	8	4.02
Hydroxycitronellal.....	148	118	472	4.00
$\alpha$ -Ionone.....	10	9	47	5.36
$\beta$ -Ionone.....	111	69	290	4.18
Ionone ( $\alpha$ - and $\beta$ -).....	38	34	101	2.95
Linalool.....	251	48	238	4.93
Linalyl acetate.....	120	89	449	5.02
Methyl- $\alpha$ -ionone.....	77	66	321	4.88
Methylnonone ( $\alpha$ - and $\beta$ -).....	52	59	264	4.47
Nerol.....	2	2	19	9.32
Rhodinol.....	8	6	59	25.73

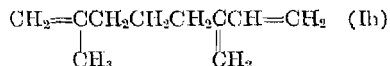
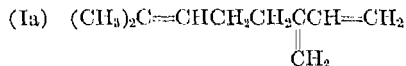
important items of commerce in the perfume, cosmetic and flavoring industries, and some find use as solvents in a wide variety of mixtures. The U.S. Tariff Commission's report for 1953 includes commercial data relative to the more important acyclic terpenoids (Table I). See also *Flavors and spices; Oils, essential; Perfumes (synthetics and isolates)*.

In general, the elucidation of the structures is based upon oxidation, reduction, ozonolysis, hydration and dehydration reactions and methods of synthesis. For many of the compounds, evidence has been obtained of isopropenyl-isopropylidene isomerism:  $\text{CH}_2=\text{C}(\text{CH}_3)-$  and  $(\text{CH}_3)_2\text{C}=\text{}$ . More recently the study of various spectra has aided in determining the presence or absence of structural isomers. Infrared measurements indicate the predominance of the isopropylidene structure in naturally occurring terpenes (6). Ultraviolet spectroscopy supports this conclusion (28) in certain cases.

Table II lists representative physical constants of the important acyclic terpenes and their derivatives, but the data are subject to revision inasmuch as many of the compounds have not been prepared in the pure condition ( $\pm 13,25$ ).

### Hydrocarbons

**Myrcene** from natural sources appears to be entirely 7-methyl-3-methylene-1,6-octadiene (Ia). However, the product obtained by dehydration of linalool gives evidence of another structure, 2-methyl-6-methylene-1,7-octadiene (Ib) (22). The ultraviolet absorption spectrum (26,28) is in reasonable agreement with both structures.



Myrcene may be identified by reduction to *dihydromyrcene*,  $(\text{CH}_3)_2\text{C}=\text{CHCH}_2\text{CH}_2\text{C}(\text{CH}_3)=\text{CHCH}_3$ , and subsequent conversion to the tetrabromide (10). When heated in a sealed tube at  $300^\circ\text{C}$ ., myrcene is converted to *dimyrcene* (containing camphorene) (see p. 758). Myrcene polymerizes even on standing at room temperature, and for this reason the material should be stored at reduced temperature ( $3^\circ\text{C}$ .) or else preserved with an inhibitor such as 0.1% *p*-tert-butylpyrocatechol (23). The action of sulfuric acid and acetic acid at room temperature yields *myrcenol*, apparently a tertiary alcohol (ref. 25, p. 68). When treated with selenium dioxide, myrcene is converted to another alcohol which also has been described as a "myrcenol." The relationship of the two has not been established, but in all probability the latter is a mixture of primary and secondary alcohols.

Myrcene may be prepared by the vapor-phase isomerization of  $\beta$ -pinene (15) (see p. 727) or of turpentine fractions rich in  $\beta$ -pinene (10); yields of 85% have been reported from this method (29). It polymerizes readily, and when  $\beta$ -pinene is thermally isomerized in the liquid phase only polymeric myrcene and limonene are obtained in significant quantities (18). A technical grade (75% myrcene),  $d_{15.5}^{20} 0.807$ , is available.

**Ocimene** has long been represented as 3,7-dimethyl-1,3,7-octatriene (IIa). More recently an isopropylidene structure, 3,7-dimethyl-1,3,6-octatriene (IIb) has been proposed (14). It has not been obtained in a pure state.

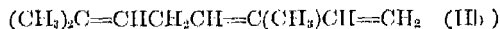
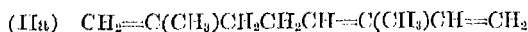


TABLE II. Acyclic Monoterpenoids and Their Derivatives.

Compound	Formula	Chief natural sources	B.p.		$n_D$	d	Specific rotation	M.p. of derivatives, °C.
			°C.	Mm. Hg				
			Hydrocarbons					
Allo-ocimene	$C_{10}H_{16}$	<i>Ocimum basilicum</i> Linn., <i>Homoranthus flavescens</i> , <i>Evoida rutacarpa</i>	81	12	1.5424 <sup>25</sup>	0.8083 <sup>25</sup>	0	Maleic anhydride adduct, 83-84
Cryptotenene	$C_{10}H_{16}$	<i>Cryptotaenia japonica</i> Hassk.	67-8	15	1.4748 <sup>25</sup>	0.8128 <sup>25</sup>	+2.66°	No solid derivatives described
Geraniolene	$C_9H_{16}$	Unknown	142-3	760	1.4368 <sup>b</sup>	0.757 <sup>29</sup>	0	No solid derivatives described
Myrcene	$C_{10}H_{16}$	Oil of bay; verbena oil, oil of hops	166-8 65.5	760 20	1.4682 <sup>25</sup>	0.7921 <sup>25</sup>	0	1,4-Naphthoquinone adduct, 80-81.5; maleic anhydride adduct, 84-85; carboxylic acid, 122-123
Dihydromyrcene	$C_{10}H_{16}$	Unknown	166-8 67-67.5	761 20	1.4507 <sup>20</sup>	0.7755 <sup>30</sup>	0	Tetrabromide, 88
Ocimene	$C_{10}H_{16}$	<i>Ocimum basilicum</i> Linn., <i>Homoranthus flavescens</i> , <i>Evoida rutacarpa</i>	176-8 70-74	<sup>a</sup> 20	1.4831 <sup>25</sup>	0.8031 <sup>15</sup>	0	No crystalline derivatives listed; reduction to dihydromyrcene; hydration to ocimenol, phenylurethan, 72
			Alcohols					
Bupleurol	$C_{10}H_{16}O$	<i>Bupleurum fruticosum</i> L.	209-210	762	1.4508 <sup>b</sup>	0.8490 <sup>17</sup>	0	Phenylurethan, 45; silver salt of acid phthalate, 135 (dec.)
d-Citronellol	$C_{10}H_{16}O$	Java citronella oil, oil of geranium, Spanish verbena, gland secretion of alligator (yacarol)	119-121	20	1.45641-1.45791 <sup>22</sup>	0.866 <sup>17</sup>	+2.7 to 2.3° +6.8° for yacarol	Allophanate, 105-106; silver phthalate, 125-126; citronellyl pyruvate semicarbazone, 110-111

<i>l</i> -Citronellol (rhodinol)	$C_{10}H_{18}O$	Reunion geranium oil, rose oil, pink geranium oil	225-6 114-5	764.5 12	1.459-1.463 <sup>22</sup>	0.862-0.869 <sup>15</sup>	-4.2°	Allophanate, 106-107
Geraniol	$C_{10}H_{18}O$	Palmarosa, rose oil, citro- nella oil, geranium oil, coriander, ylang-ylang, neroli	230 121	757 18	1.476-1.479 <sup>20</sup>	0.8812 <sup>14</sup>	0	Acid phthalate, 47; di- phenylurethan, 82; allo- phanate, 124; di-2-naph- thylurethan, 104-107
Lavandulol	$C_{10}H_{18}O$	French lavender oil	94-5	13	1.4683 <sup>17</sup>	0.8785 <sup>17</sup>	-10.2°	Allophanate, 119-120; 3,5- dinitrobenzoate, 59-60; anthraquinone-2- carboxylate, 62-63
<i>d</i> -Linalool (coriandrol)	$C_{10}H_{18}O$	Rosewood oil, coriander oil, linaloe seed oil	198-9 85-7	760 10	1.468 <sup>20</sup>	0.870 <sup>15</sup>	+19.2°	Phenylurethan, 65-66; 1- naphthylurethan, 53
<i>l</i> -Linalool (licareol)	$C_{10}H_{18}O$	Bergamot oil, lavender oil, petitgrain, linaloe wood oil, oil of shiu	198-9 85-7	760 10	1.468 <sup>20</sup>	0.870 <sup>15</sup>	-20.7°	Phenylurethan, 65-66; 1- naphthylurethan, 53
Myrcenol	$C_{10}H_{18}O$	Lemon oil	99-101	10	1.4806 <sup>15</sup>	0.9042 <sup>15</sup>	—	Phenylurethan, 68; alloph- anate, 110-111
Nerol	$C_{10}H_{18}O$	Neroli, bigarade, petit- grain, rose oil, lavender oil, oil of <i>Helichrysum</i> <i>angustifolium</i>	224-5	755	1.462 <sup>20</sup>	0.8813 <sup>15</sup>	0	Tetrabromide, 116-118; allophanate, 101.5; di- phenylurethan, 52.5
Aldehydes								
Citral	$C_{10}H_{16}O$	Lemongrass oil, Java citronella oil, lemon and lime oils	228-9 117-9	<sup>a</sup> 20	1.482-1.489 <sup>20</sup>	0.892-0.895 <sup>15</sup>	0	Thiosemicarbazone, 107- 108; 3-nitrobenzohydra- zone, 100-101; semiox- amazone, 190-191; nitro- guanyldiazone, 135- 136.5
Citral $\alpha$ (geranial)	$C_{10}H_{16}O$	Lemongrass oil, Java citronella oil, lemon and lime oils	110-12	12	1.4891 <sup>20</sup>	0.8898 <sup>20</sup>	0	Semicarbazone, 164; citryl- idenecyanoacetic acid, 122; $\beta$ -naphthocineho- minic acid deriv., 202

(Continued)

TABLE II. Acyclic Monoterpenoids and Their Derivatives (Concluded).

Compound	Formula	Chief natural sources	B.p.		$n_D$	d	Specific rotation	M.p. of derivatives, °C.
			°C.	Mm. Hg				
Aldehydes ( <i>Continued</i> )								
Citral <i>b</i> (neral)	$C_{10}H_{16}O$	Lemongrass oil, Java citronella oil, lemon and lime oils	102-4	12	1.4900 <sup>20</sup>	0.891 <sup>15</sup>	0	Semicarbazone, 171; citryl-idenecyanoacetic acid, 95; $\beta$ -naphthocinchoninic acid deriv., 202
<i>d</i> -Citronellal	$C_{10}H_{16}O$	Oil of citronella, <i>Eucalyptus citriodora</i>	205-6 89-91	760 14	1.448 <sup>20</sup>	0.8554 <sup>20</sup>	+12.3°	Semicarbazones, 77.5, 86; <i>dl</i> -citronellal semicarbazone, 96
<i>l</i> -Citronellal (rhodinol)	$C_{10}H_{16}O$	<i>Leptospermum frutescens</i> (var. <i>citratum</i> )	205-8	<sup>a</sup>	1.44791 <sup>20</sup>	0.8567 <sup>15</sup>	-3°	Semicarbazone, 91-2; $\beta$ -naphthocinchoninic acid deriv., 225; citronellyl-idenecyanoacetic acid, 137-8; 2,4-dinitrophenylhydrazones, 77-8
Ketones								
Artemesia ketone	$C_{10}H_{16}O$	<i>Artemesia annua</i> L.	182	760	1.4685 <sup>15,5</sup>	0.8906 <sup>14</sup>	0	Semicarbazone, 95-6; azide, 156
Isocarfenesia ketone	$C_{10}H_{16}O$	<i>Artemesia annua</i> L.	182-3	760	1.4188 <sup>b</sup>	0.8711 <sup>17</sup>	0	Semicarbazone (hydrated), 70-2; (anhydrous), 103-4
Tagetone	$C_{10}H_{16}O$	Tagetes oil ( <i>Tagetes glauca</i> <i>dulifera</i> )	205-10 63	760 3-4	1.4895 <sup>21</sup>	0.8803 <sup>15,5</sup>	0	Semicarbazone, b <sub>2</sub> , 216; semicarbazone of the completely saturated alcohol, 92-3

<sup>a</sup> Pressure not indicated.<sup>b</sup> Temperature not indicated.



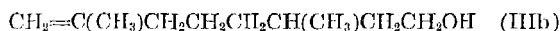
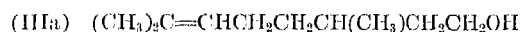
Ocimene is quite reactive and undergoes oxidation and resinification with ease. On heating it is isomerized to allo-ocimene. It is best stored under nitrogen at about  $-20^{\circ}\text{C}$ . Ocimene may be prepared by the vapor-phase thermal isomerization of  $\alpha$ -pinene under special conditions (14). It has no important uses, but it is present in estragon oil, an ingredient of aromatic vinegars.

**Allo-ocimene** (3,7-dimethyl-2,4,6-octatriene),  $(\text{CH}_3)_2\text{C}=\text{CHCH}=\text{CHC}(\text{CH}_3)=\text{CHCH}_3$  (8; ref. 25, p. 21; 28), may be prepared by thermal isomerization of  $\alpha$ -pinene (9,10) or of ocimene (14). Two stereoisomeric compounds, probably of *trans*- $\text{C}_4$ -*cis*- $\text{C}_6$ - and *trans*- $\text{C}_4$ -*trans*- $\text{C}_6$ - configuration, are produced in this manner. Either form yields the same adduct with maleic anhydride (17). Pyrolysis of allo-ocimene causes cyclization to  $\alpha$ - and  $\beta$ -pyronenes (11) (see p. 706). Allo-ocimene is available commercially as a by-product of dipentene synthesis from  $\alpha$ -pinene (p. 723).

### Alcohols

A few of the acyclic alcohols are of considerable commercial importance.

**Citronellol** (2,3-dihydrogeraniol) gives evidence of both an isopropylidene structure (IIIa), 3,7-dimethyl-6-octen-1-ol, and of an isopropenyl structure (IIIb), 3,7-dimethyl-7-octen-1-ol. Ozonolysis (7,12) and spectroscopic data indicate that the material consists almost entirely of (IIIa) (2,21,27), and the chemical evidence for (IIIb) may be attributed to the ease of isomerization during reaction.



It was once believed that the two optically active forms were structural isomers (ref. 25, p. 28), and early investigators designated the impure levorotatory material variously as rhodinol, roseol, and reuniol in distinction from the dextrorotatory compound citronellol. Later it was shown by ozonolysis that the two forms are stereoisomers (7,12) and that rhodinol, roseol, and reuniol are identical when purified; the designation "rhodinol" was then applied to the pure levo compound. The term rhodinol now bears a special connotation in the trade, referring to the comparatively expensive mixture of *levo*-citronellol and geraniol obtained from rose or geranium oils, while the term citronellol refers to the dextrorotatory material commonly obtained from Java citronella oil or from citronellal by reduction.

Citronellol undergoes reaction at either its hydroxyl or its olefin group. It therefore forms such alcohol derivatives as the allophanate, acid phthalate, pyruvate, acetate, and formate. The hydroxyl group does not enter into reaction with the halogen acids, however, although the chloride is formed at elevated temperatures together with the olefinic addition product.

Dilute sulfuric acid produces a glycol by olefinic reaction but fails to effect cyclization. Even in concentrations of more than 50%, sulfuric acid is ineffective in this respect, although much polymerization is noted. Other olefinic reactions include the addition of hydrogen chloride in acetic acid to yield an unstable product, catalyzed hydrogenation to 3,7-dimethyl-1-octanol, and the addition of sodium bisulfite.

According to conditions, oxidation yields a variety of compounds, including citronellal, citronellie acid, isopulegol, menthone,  $\beta$ -methyladipic acid, hydroxy and ketonic acids.

Citronellol (dextrorotatory) is isolated by treatment of the oil, for example, Java

citronella oil, with alcoholic potassium hydroxide at 160°C. and subsequent decomposition of the alcoholate, or commercially by reduction of citronellal. The alcohol is sold in bottles and drums and is also available as the acetate, propionate, and butyrate.

*levo*-Citronellol can be separated from the accompanying geraniol in geranium oils by formation of the acid phthalate, formate, or "chloro citronellyl phosphoric ester" by reaction with phosphorus trichloride in ether solution under such conditions that the geraniol is destroyed during esterification (ref. 13, I, p. 180). The mixture "rhodinol," containing *levo*-citronellol, is sold in 5-lb. cans.

Citronellol is used in many heavy and floral perfumes including rose, geranium, and lilac. It is also used in soaps and has been recommended as a component for honey flavors. Rhodinol is used to bolster fine-quality rose compositions and light florals, but its cost prohibits its use in cheap preparations.

**Geraniol** is structurally isomeric with linalool and geometrically isomeric with nerol. Oxidation yields evidence of an isopropylidene structure (IVa), *trans*-3,7-dimethyl-2,6-octadien-1-ol, and of an isopropenyl structure (IVb), *trans*-3,7-dimethyl-2,7-octadien-1-ol (ref. 25, p. 40). Spectroscopic data indicate that the material consists almost entirely of (IVa) (2,27). However, isomerization evidently occurs with considerable ease, and both forms may be present in a reaction.



The stereochemical formulas of geraniol and nerol (and therefore of the related aldehydes, geranial and neral—see p. 716) are based upon the relative ease of cyclization of nerol in the presence of mineral acids to terpineol and terpin hydrate, a consequence of nerol's stereochemically favorable configuration, assumed to be *cis* (ref. 25, p. 46). Geraniol, which must isomerize to nerol before cyclization, yields terpineol much less rapidly and therefore is assigned a *trans* configuration.

Geraniol is also cyclized by anhydrous hydrogen chloride or hot activated charcoal to dipentene (limonene). If the hydroxyl group is esterified, cyclization with sulfuric or phosphoric acid follows another course and yields a mixture of the isomeric  $\alpha$ - and  $\beta$ -cyclogeranyl esters (Va and Vb), which may be hydrolyzed to yield the isomeric *cyclogeraniols*. The proportion of either ester may be regulated by the choice of acid, sulfuric acid disposing toward the production of the  $\beta$ -form and phosphoric acid toward the  $\alpha$ -form.



Isomerization without cyclization is observed in the conversion of geraniol to linalool on simple heating in the absence of acid. Geraniol is comparatively stable toward alkali, but concentrated alkali at 150°C. causes decomposition to 6-methyl-5-hepten-2-one together with its reduction product, 6-methyl-5-hepten-2-ol.

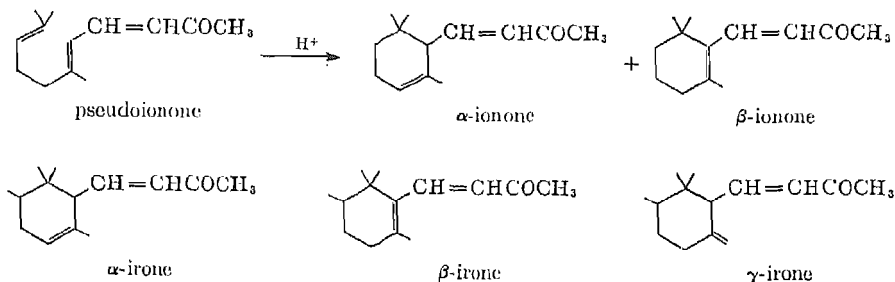
It is decomposed by phthalic anhydride at 150°C., formic acid, and related agents in the isolation of *levo*-citronellol (see above). Permanganate oxidation yields acetone and levulinic acid.

Geraniol is present in a large number of essential oils. The best grade is obtained from palmarosa oil (which is largely composed of this alcohol), although Java-type citronella oil is an important source of a commercially valuable but inferior product.





called *pseudoionone a* and *b* (16). Cyclization of the pseudoionones in the presence of acids gives a mixture of  $\alpha$ - and  $\beta$ -ionones (4-(2,6,6-trimethyl-2(and 1)-cyclohexenyl)-3-buten-2-ones); thus, for the isopropylidene forms:



Phosphoric acid gives chiefly  $\alpha$ -ionone, and sulfuric acid chiefly  $\beta$ -ionone. The ionones can also be prepared by condensing the cyclocitral (see below) with acetone. Condensation of citral with methyl ethyl ketone instead of acetone gives "methylpseudoionones," which can be cyclized to "methylionones," containing the side chain  $CH=CHCOCH_2CH_3$  and also  $CH=C(CH_3)COCH_3$ . (See Vol. 10, pp. 23, 30.) Other methylionones, named *irones*, contain the additional methyl group attached to the ring para to the single methyl group and have been synthesized by condensing the corresponding methyleyclocitral with acetone and by several steps starting with 5,6-dimethyl-5-hepten-2-one. Three isomers,  $\alpha$ -,  $\beta$ -, and  $\gamma$ -irones, are known, and each of these exists in geometrically isomeric forms. The mixture of irones occurring in iris root is now thought to consist of undetermined proportions of the alpha and gamma isomers (ref. 3, p. 505). These isomers, on treatment with acid or alkalis, readily go over into the beta form (20), which has a violet-like odor similar to that of the ionones rather than the fragrance of the iris root.

A reverse aldol condensation of citral occurs when it is heated with warm alkali; acetaldehyde and 6-methyl-5-hepten-2-one are produced.

Catalytic hydrogenation yields any of the following products according to conditions: citronellal, citronellol, geraniol, 3,7-dimethyl-1-octanol, and 2,6-dimethyloctane. Olefinic addition of bromine is also observed, but the tetrabromide is unstable. Mineral acids also react poorly at the olefinic group, producing instead cyclization to hydrocarbons, *p*-cymene or menogerene (1,4(8),5-*p*-menthatricene). Cyclization to the isomeric  $\alpha$ - and  $\beta$ -cyclocitral (2,6,6-trimethyl-2(and 1)-cyclohexene-1-carboxaldehydes) cannot be accomplished directly, but these compounds, principally  $\beta$ -cyclocitral, are formed by alkaline hydrolysis of the  $\alpha$ - and  $\beta$ -cyclocitrylideneacyanoacetic acids obtained from the cyclization of the citrylideneacyanoacetic acids in the presence of sulfuric acid. The cyclocitral may also be obtained by steam distillation of the Schiff bases of citral. Citral also undergoes cyclization with acetic anhydride to form an enol acetate, which on hydrolysis yields an isomer of citral, *isocitral*, a compound of undetermined structure but presumably 3,6-dimethyl-3,6-octadienal or its isopropenyl isomer (24).

Citral is readily oxidized, and the following compounds may be formed according to experimental conditions; geranic acid, 6-methyl-5-hepten-2-one, acetone, and levulinic acid. Oxidation occurs at a moderately rapid rate even in the air, and this must be considered in storage of the material.

Citral is found in numerous essential oils, notably in lemongrass oil, of which it constitutes about 80%, the bulk of this (90%) being citral *a*. Citral *a* may be obtained from its essential oils by isolation and subsequent decomposition of its normal sodium bisulfite addition product. Citral *b* is isolated by prior removal of citral *a* as

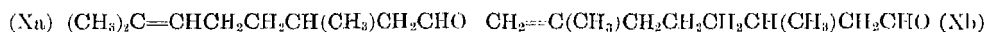
the cyanoacetic acid condensation product. Although both aldehydes react with this acid, citral *a* reacts more rapidly, and the unreacted citral *b* may be recovered from the reaction mixture. A commercial method for synthesizing citral (with linalool as one of the by-products) from an acetylene derivative has been announced, with no details.

Citral is offered in pure, c.p. grades (98–100%) in bottles and 50-lb. cans;  $\alpha$ -ionone and  $\beta$ -ionone in regular and extra grades (85–100%) in 25-lb. cans; methylionone in a standard grade in cans and drums, and  $\alpha$ - and  $\beta$ -methylionones in grades of 83–90% in cans.

Citral, that is, the mixture, is of importance in the flavoring and perfumery trade for its lemon and verbena effects. Its condensation products with acetone, the pseudoionones, are also of considerable importance in the preparation of the ionones, which are used in almost all types of perfumes for their violet-like fragrance. Ione is also an important perfume constituent, but it is expensive. See also Vol. 10, p. 23.

Pharmaceutically citral is said to have value as an antihistaminic and as an analgesic in ophthalmology (1).  $\beta$ -Ionone is the starting material in the most widely used synthetic method for vitamin A (see *Vitamins*).

**Citronellal** corresponds to the alcohol citronellol and like the alcohol gives evidence of an isopropylidene form (Xa), 3,7-dimethyl-6-octenal, and an isopropenyl form (Xb), 3,7-dimethyl-7-octenal, with the former predominating according to spectrographic data (2,25). The levo form is sometimes called *rhodinal*.



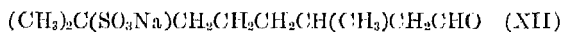
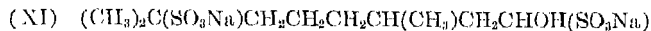
Citronellal undergoes a variety of reactions typical of its aldehydic and olefinic nature. Aldehyde reactions include the normal addition of sodium bisulfite in the cold and reactions with hydroxylamine, hydrazine, 2,4-dinitrophenylhydrazine, semicarbazide, and methanol to yield the oxime, hydrazone, 2,4-dinitrophenylhydrazone, semicarbazone, and dimethyl acetal, respectively. Aldol-like condensations are known including those with malonic acid, pyruvic acid and 2-naphthylamine, cyanoacetic acid, and acetone to yield citronellylidenemalonic acid, "citronellyl- $\beta$ -naphthoeinchonic acid," citronellylidenecyanoacetic acid, and dihydropseudoionone, respectively (ref. 25, p. 76). Two semicarbazones have been obtained from *dextro*-citronellal, and it has been suggested that these compounds may be structural isomers corresponding to the isopropylidene (Xa) and isopropenyl (Xb) forms of the aldehyde.

The aldehyde group also enters into cyclization reactions, isopulegol (*p*-8-menthen-3-ol) being formed in the presence of acids (5% sulfuric, 80% formic, or 80% phosphoric) or by ultraviolet light. Acetic anhydride produces a similar cyclization except that isopulegol is obtained as the acetate. The tendency toward cyclization is so marked that most commercial citronellal products are contaminated with isopulegol or menthone (produced on oxidation).

Oxidative reactions yield a variety of compounds according to conditions. Mild oxidation with silver oxide yields citronellic acid, and air oxidation in sunlight produces a complex mixture of acetone,  $\beta$ -methyladipic acid, isopulegol, and menthone. Peroxybenzoic acid forms a monoxide, and ozonolysis of the dimethyl acetal yields formic acid, acetone, and a number of fragmentation products indicative of the co-existence of the isopropylidene and isopropenyl forms.

Reduction may be accomplished with or without involvement of the olefinic group according to conditions. Reduction with sodium amalgam in faintly acidic medium yields citronellol, and this reaction finds commercial application in the prepa-

ration of this alcohol. Catalytic hydrogenation with platinum or palladium catalyst yields dihydrocitronellal, while the use of a nickel catalyst yields the alcohol 3,7-dimethyl-1-octanol. The addition of sodium bisulfite likewise yields a number of products according to conditions (13, I, p. 337). Whereas the normal product is obtained by carbonyl addition in the cold, if an excess of sodium bisulfite containing some sodium sulfite is used, the di-addition product (XI) is obtained. Treatment of (XI) with alkali yields a monoaddition product (XII), which is isomeric with the normal addition product but has a free aldehyde group and is incapable of regenerating the original aldehyde.



Relatively few strictly olefinic reactions are listed. Hydration to *hydroxycitronellal*,  $(CH_3)_2(OH)C(CH_2)_3CH(CH_3)CH_2CHO$ , can be accomplished with acids at low temperature if the aldehyde group is protected by the addition of sodium bisulfite (see Vol. 10, pp. 21, 29). Reactions with halogens and halogen acids have been noted, but the addition compounds formed in these reactions are unstable.

Citronellal may be separated from its essential oil by the isolation and subsequent alkaline hydrolysis of its normal (carbonyl) sodium bisulfite addition product. Inasmuch as citronellal forms resins and undergoes decomposition at high pH values, the hydrolysis must be conducted cautiously with alkali carbonate rather than hydroxides. The aldehyde may be prepared by oxidation of citronellol or by reduction of citral, although neither method is practical. Commercial citronellal is obtained by fractionation of Java-type citronella oil.

Citronellal bears a lemon-like or melissa fragrance and is a useful ingredient in low-priced commercial preparations because of its odor strength and covering power. It is also used to some extent in artificial citrus flavors. More important is the use of citronellal for the synthesis of citronellol, of hydroxycitronellal (a valued perfumery synthetic with a lily-of-the-valley note), and of *levo*-menthol by hydrogenation of isopulegol (see p. 734).

### Bibliography

- (1) Balakhovskii, S. D., Troitskaya, N. A., and Kolesnokova, N. V., *Biokhimiya*, **15**, 267 (1950); *C. A.*, **44**, 10078 (1950).
- (2) Barnard, D., Buteman, L., Harding, A. J., Koch, H. P., Sheppard, N., and Sutherland, G. B. B. M., *J. Chem. Soc.*, **1950**, 915.
- (3) Barton, D. H. R., and Harper, S. H., in Rodd, *Chemistry of Carbon Compounds*, Elsevier, Houston, Tex., and Amsterdam, 1953, Vol. 11B, ch. XIII.
- (4) Bedoukian, P. Z., *Perfumery Synthetics and Isolates*, Van Nostrand, N.Y., 1951.
- (5) Bertram, J., and Gildemeister, E., *J. prakt. Chem.*, [2], **53**, 233 (1896).
- (6) Carroll, M. F., Mason, R. G., Thompson, H. W., and Wood, R. C. S., *J. Chem. Soc.*, **1950**, 3457.
- (7) Doeuvre, J., *Parfums de France*, **12**, 197 (1934).
- (8) Fischer, F. G., and Lowenberg, K., *Ber.*, **66**, 669 (1933).
- (9) Fugitt, R. C., and Hawkins, J. E., *J. Am. Chem. Soc.*, **67**, 242 (1945).
- (10) Goldblatt, L. A., and Palkin, S., *J. Am. Chem. Soc.*, **63**, 3517 (1941).
- (11) Goldblatt, L. A., and Palkin, S., *J. Am. Chem. Soc.*, **66**, 655 (1944).
- (12) Grignard, V., and Doeuvre, J., *Compt. rend.*, **187**, 270 (1928).
- (13) Guenther, E., and Althausen, D., *The Essential Oils*, Van Nostrand, N.Y., 1949, Vols. I and II.
- (14) Hawkins, J. E., and Hunt, H. G., *J. Am. Chem. Soc.*, **73**, 5379 (1951).

- (15) Hawkins, J. E., and Vogh, J. W., *J. Phys. Chem.*, **57**, 902 (1953).
- (16) Hibbert, H., and Cannon, L. T., *Org. Syntheses*, **23**, 78 (1943).
- (17) Hopfield, J. J., Hall, S. A., and Goldblatt, L. A., *J. Am. Chem. Soc.*, **66**, 115 (1944).
- (18) Hunt, H. G., and Hawkins, J. E., *J. Am. Chem. Soc.*, **72**, 5618 (1950).
- (19) Jones, H. A., and Wood, J. W., *Ind. Eng. Chem.*, **34**, 488 (1942).
- (20) Moneriet, R. W., *Perfumery Essent. Oil Record*, **40**, 320, 337 (1949).
- (21) Naves, Y. R., *Bull. soc. chim. France*, [5], **18**, 505 (1951).
- (22) Pigulevskii, G. V., and Prokudina, N. L., *Doklady Akad. Nauk. S.S.S.R.*, **67**, 282 (1949); *C.A.*, **44**, 1938 (1950).
- (23) Runckel, W. J., and Goldblatt, L. A., *Ind. Eng. Chem.*, **38**, 749 (1946).
- (24) Schmidt, H., *Ann. Repts. Schimmel & Co.*, **1938**, 124; *Ber. Schimmel & Co. Akt.-Ges.*, **1939**, 114.
- (25) Simonsen, J. L., and Owen, L. N., *The Terpenes*, 2nd ed., University Press, Cambridge, England, 1947, Vol. I, pt. I.
- (26) Sutherland, M. D., and Wilson, S. J., *Univ. Queensland Papers, Dept. Chem.*, **1**, No. 38 (1950).
- (27) Thompson, H. W., and Whiffen, D. H., *J. Chem. Soc.*, **1948**, 1412.
- (28) Walker, R. D., Jr., and Hawkins, J. E., *J. Am. Chem. Soc.*, **74**, 4209 (1952).
- (29) U.S. Pat. 2,507,546 (May 16, 1950), T. R. Savich and L. A. Goldblatt (to U.S.A.).

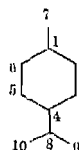
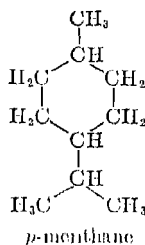
J. E. HAWKINS AND E. G. RIETZ

## MONOTERPENOIDS—CYCLIC

### Monocyclic Hydrocarbons

The monocyclic terpenes constitute a large group of isomeric compounds which are of interest as such and as the parent hydrocarbons for a variety of derivatives containing functional groups.

The monocyclic terpene hydrocarbons are chiefly compounds having the carbon skeleton of *p*-menthane (1-methyl-4-isopropylcyclohexane):



*p*-Menthane and several of the other terpenes and terpene derivatives exist in *cis* and *trans* forms which differ enough in physical properties to allow isolation by physical means. Those terpenes containing one or more asymmetric carbons also exhibit optical isomerism.

The monocyclic terpenes for which no historical names have been established are named systematically as menthenes or menthadienes using the fixed numbering system shown.

The skeleton structural formulas of the principal monocyclic terpenes are given in Figure 1.



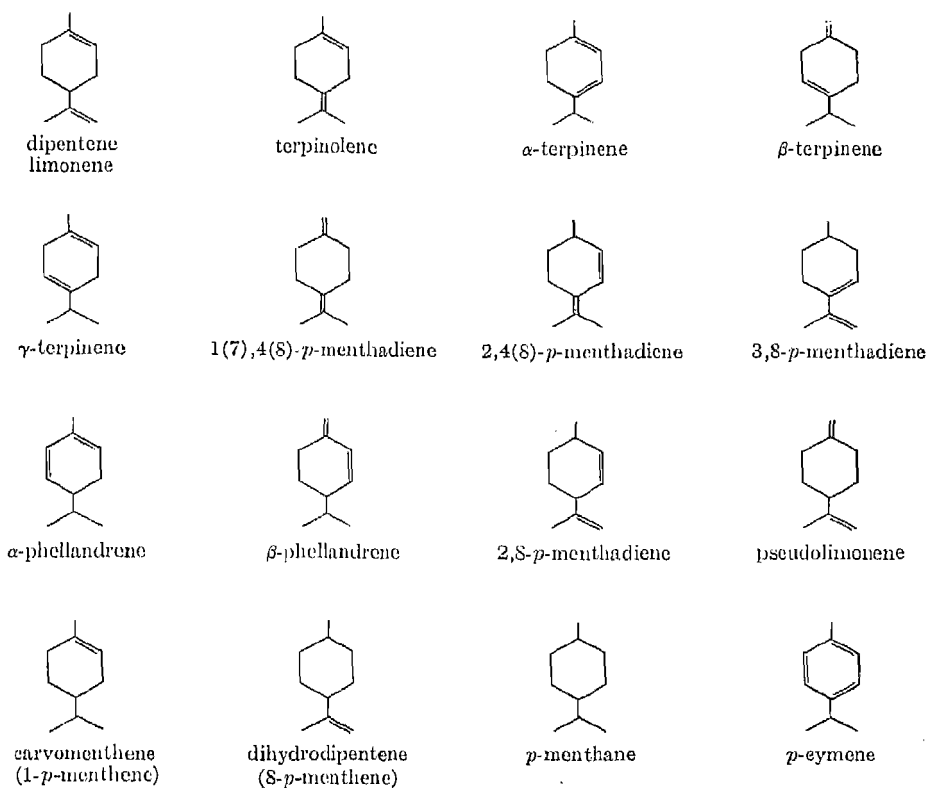


Figure 1.

## PHYSICAL AND CHEMICAL PROPERTIES

The difficulty of obtaining terpenes free from isomeric compounds has hindered attempts to obtain reliable physical properties. The use of more efficient distillation equipment coupled with improved methods of instrumental analysis has, however, allowed a considerable improvement. Some physical properties of the principal monocyclic terpenes are reported in Table I (6,21,22).

The chemical properties of monocyclic terpenes are not unique but rather are those that might be expected from their structures. In the case of the menthenes and menthadienes, the majority of the reactions are those that involve the double bonds or the allylic hydrogens (hydrogens on carbons alpha to double bonds). Catalytic hydrogenation yields *cis*- and *trans*-*p*-menthane. Addition of halogens or hydrogen halides yields the corresponding alicyclic halides; free-radical chlorination yields polyhalides. Heating with sulfur forms complex sulfurized compounds. This reaction is the basis for sulfurized terpene extreme-pressure lubricant additives. Treatment with many acids, acid clays, and metallic halides yields isomerized olefins and dimeric terpenes. Reaction with oxygen yields hydroperoxides which frequently react further to yield alcohols, ketones, and acids. *p*-Menthane hydroperoxide is produced commercially by this reaction. Reaction with maleic anhydride (see Vol. I, p. 527; Vol. 8, p. 682) yields Diels-Alder adducts of the conjugated diolefins. The nonconjugated diolefins react probably by isomerization to conjugated diolefins and by re-

TABLE I. Physical Properties of Monocyclic Terpene Hydrocarbons.

Compound	B.p., °C.		$n_D^{20}$	$d_4^{20}$
	760 mm.	100 mm.		
Dipentene	176.5	110 <sup>a</sup>	1.4730 <sup>a</sup>	0.8447 <sup>a</sup>
Terpinolene	186 <sup>a</sup>	120 <sup>a</sup>	1.4895 <sup>a</sup>	0.8620 <sup>a</sup>
$\alpha$ -Terpinene	175	108	1.4790	0.8353 <sup>13</sup>
$\beta$ -Terpinene	—	—	1.4750 <sup>25</sup>	0.8356 <sup>25</sup>
$\gamma$ -Terpinene	—	116 <sup>a</sup>	1.4754	0.851
2,4(8)- <i>p</i> -Menthadiene	—	120 <sup>a</sup>	1.5057 <sup>a</sup>	0.8592 <sup>a</sup>
3,8- <i>p</i> -Menthadiene	—	117.5 <sup>a</sup>	1.4874 <sup>25a</sup>	0.8498 <sup>25</sup>
$\alpha$ -Phellandrene	—	—	1.4702 <sup>25</sup>	0.8284 <sup>25</sup>
$\beta$ -Phellandrene	—	—	1.4851 <sup>25</sup>	0.8375 <sup>25</sup>
Carvomenthene	176 <sup>a</sup>	110 <sup>a</sup>	1.4572 <sup>a</sup>	0.8490 <sup>30</sup>
<i>p</i> -Cymene	177	110 <sup>a</sup>	1.4905 <sup>a</sup>	0.857
<i>cis-p</i> -Menthane	—	105	1.4431	0.8084 <sup>a</sup>
<i>trans-p</i> -Menthane	170 <sup>a</sup>	103	1.4367 <sup>a</sup>	0.7938 <sup>a</sup>
2- <i>p</i> -Menthene	169	—	1.4490	—
3- <i>p</i> -Menthene	169	102 <sup>a</sup>	1.4519	—
4(8)- <i>p</i> -Menthene	176	110 <sup>a</sup>	1.4689	—
8- <i>p</i> -Menthene	169	—	1.4454	0.819

<sup>a</sup> Values from the Laboratories of Hercules Powder Co.

action with the allylic hydrogens (see Vol. 8, p. 688). Reaction with aromatic hydrocarbons and phenols in the presence of Friedel-Crafts catalysts yields alkylated compounds. The menthadienes can be dehydrogenated to *p*-cymene or disproportionated to *p*-cymene and *p*-menthane. Hydration with sulfuric acid catalyst yields alcohols and glycols. Addition of nitrosyl chloride yields the nitrosochlorides, which are used to characterize terpenes (see Vol. 9, p. 468). Ozonolysis cleaves the double bond to yield aldehydes, ketones, and acids.

Specific compounds have additional reactions. For example, dipentene can be cracked to yield a mixture including isoprene. *p*-Cymene can be further dehydrogenated to yield  $\alpha$ ,*p*-dimethylstyrene.

#### OCCURRENCE

The most important monocyclic terpene industrially is limonene and its optically inactive (*dl*- or racemic) form dipentene. *dextro*-Limonene (carvene, hesperidene) and *levo*-limonene occur in many essential oils such as dill, caraway, and star anise. The principal commercial sources are the oils of orange, grapefruit, and lemon from which it may be obtained readily in over 90% purity. Dipentene occurs in a variety of essential oils such as bergamot, citronella, and nutmeg. The chief domestic sources are wood and sulfate turpentine (*q.v.*) from the southern pine (*Pinus palustris* and *P. caribaea*). Dipentene is formed together with other monocyclic terpenes as a major by-product in many acid-catalyzed reactions of  $\alpha$ -pinene such as its isomerization to camphene by an acidic clay. Dipentene is also formed together with acyclic terpenes by thermal cracking of  $\alpha$ -pinene.

Several of the sources of dipentene are also sources of other monocyclic terpenes. Thus, the monocyclic terpene fraction extracted from pinewood stumps contains terpinolene, *p*-cymene, *p*-menthanes, 2,4(8)-*p*-menthadiene, and  $\alpha$ -terpinene, as well as dipentene and small amounts of other isomers. The monocyclic terpenes formed by

acid-catalyzed reactions of  $\alpha$ -pinene contain terpinolene, 2,4(8)-*p*-menthadiene,  $\alpha$ -terpinene, and  $\gamma$ -terpinene in addition to dipentene.

#### MANUFACTURE

*From Orange Oil.* With the increases in the amount of citrus fruits that are processed to produce liquid or frozen canned juices, orange oil (chiefly *dextro*-limonene) from the peel has become available in moderate quantities. The volume of orange oil produced in 1951 has been estimated at 2,600,000 lb. Cold-pressed citrus oil is obtained from whole oranges by breaking the oil sacs or by crushing the peel. Distilled orange oils are obtained by vacuum-stripping citrus juices or by distilling citrus press liquor which is removed during the production of dry citrus pulp for cattle feed. Details of the procedure are given in a bulletin of the Florida Agriculture Experiment Station (13).

*From Pine Stumps.* The extraction of rosin and terpenes from wood stumps is described under *Rosin and rosin derivatives* (see Vol. 11, pp. 780-81). The total extract is distilled to yield the extracting solvent, bicyclic terpenes, monocyclic terpenes, pine oil, and the residual crude rosin. The monocyclic terpene fraction may be fractionally distilled under a variety of conditions to yield **dipentene**, **terpinolene**, and other fractions.

*From Other Sources.* Dipentene can be produced from  $\alpha$ -pinene by thermal cracking. The by-products include allo-ocimene and pyronenes. (See pp. 713, 729.) Dipentene is also formed as a by-product in the majority of acid-catalyzed reactions of  $\alpha$ -pinene such as isomerization to camphene and hydration to synthetic pine oil. The acid conditions, however, are usually drastic enough to produce other by-product terpenes and particularly  $\alpha$ - and  $\gamma$ -terpinene.

*p*-Menthane and *p*-cymene have been produced by disproportionation of mixed monocyclic terpenes with catalysts such as platinum or palladium. *p*-Menthane has been produced by hydrogenation of monocyclic terpenes using a nickel catalyst.

#### ECONOMIC ASPECTS

During World War II steam-distilled dipentene had a ceiling price of \$0.56 per gallon for carloads of drums delivered in the East (U.S.). Prices since the war have fluctuated widely as illustrated by the quotations below, also for carloads of drums (18):

Date	Price, \$/gal.
July 1947	0.80 warehouse, N.Y.C.
July 1951	0.35 works, South
July 1954	0.64 works, South

The production of dipentene and other monocyclic terpenes is given in Table II (15).

#### ANALYSIS

Terpene hydrocarbon mixtures are characterized by A.S.T.M. boiling range, refractive index, specific gravity, bromine number, kauri-butanol value (see Vol. 11, p. 676), and other common physical and chemical constants. Before the advent of instruments such as the infrared and ultraviolet spectrophotometers, the analyses of terpene mixtures for individual components required the preparation of characteristic

TABLE II. U.S. Production of Monocyclic Terpenes.

Naval stores years <sup>a</sup>	Dipentene, thousand gallons	Other monocyclic hydrocarbons, thousand gallons
1942-43	1,227	1,797
1943-44	920	1,745
1944-45	932	1,686
1945-46	970	1,686
1946-47	1,306	2,006
1947-48	1,349	1,882
1948-49	1,309	1,974
1949-50	1,486	2,202
1950-51	2,232	2,527
1951-52	1,962	2,949
1952-53	1,795	2,361

<sup>a</sup> April to March.

derivatives with maleic anhydride, nitrosyl chloride, bromine, hydrogen chloride, or other reagents. The preparation of these derivatives in some cases serves also as a method for separation, although distillation is frequently needed before identification.

Although instrumental analysis has simplified the problem, it is still frequently necessary to use all the tools at hand to obtain a satisfactory material balance. One of the largest problems is the preparation of suitable standards. To obtain a quantitative analysis by ultraviolet, infrared, or mass spectroscopy it is necessary to have samples of the components in high purity. These reference standards should be stored in glass in the absence of light, air, and heat. Analysis of simple mixtures can sometimes be obtained without resorting to separation techniques. For example, where only one component contains conjugated unsaturation, its amount may be determined by ultraviolet analysis. Infrared absorption analysis is of more general usefulness but is generally less accurate because of the high probability of interfering absorption bands. The mass spectrometer is of general usefulness but is of particular advantage where the desired component has a different mass from the other components of the mixture. Thus, *p*-menthane as a contaminant in pinane can be quantitatively determined if the *cis-trans* isomer ratio is known. In most cases a more accurate figure is obtained by fractional distillation prior to analysis. The efficiency of fractionation required will,

TABLE III. Typical Physical Properties of Commercial Dipentenene.

Property	Commercial dipentenene		
	A	B	C
$d_{4}^{15.5}$	0.8518	0.8510	0.851
$n_D^{20}$	1.4739	1.4735	1.475
Unpolymerized residue, %	1.4	3.0	1.0
Flash point, °F.	126.0 <sup>a</sup>	130	117 <sup>b</sup>
Kauri-butanol value	62	63	70
Distillation range, °C.			
5%	176.0	174.0	175
50%	177.3	177.0	176
95%	181.0	183.0	178

<sup>a</sup> Cleveland open cup.<sup>b</sup> Tag open cup.

of course, vary with the mixtures, but usually the maximum efficiency available up to at least 100 plates is not excessive. This increases manyfold the cost of analysis and, where repeated analyses are to be carried out on similar materials, the method is not practical. Even in these cases, fractional distillation should be used once to establish what components are present and the accuracy of the analysis on the original mixture.

*Typical Analyses.* The physical properties of three commercial dipentenes are given in Table III. The properties of additional terpene solvents may be found in manufacturers' bulletins (5,7,11,17,23).

The chemical composition of a typical commercial dipentene is:

Component	Amount, %
$\alpha$ - and $\beta$ -Pinene	5
<i>p</i> -Menthane	14
$\alpha$ -Terpinene	5
<i>p</i> -Cymene	17
Dipentene	51
Terpinolene	5
2,4(8)- <i>p</i> -Menthadiene	2
Fenchone	1

The physical properties of three commercial monocyclic terpene mixtures are given in Table IV.

TABLE IV. Typical Physical Properties of Solvent-Grade Monocyclic Terpenes.

Property	Commercial terpene solvents		
	D	E	F
$d_{15.6}^{15.6}$	0.8603	0.8505	0.8754
$n_D^{20}$	1.4755	1.4730	1.4802
Unpolymerized residue, %	0.5	1.8	—
Flash point, °F.	130 <sup>a</sup>	—	136
Kauri-butanol value	70	—	128
Distillation range, °C.			
5%	175.8	169.8	180.6
50%	178.4	173.4	185.4
95%	187	189.0	195.0

<sup>a</sup> Cleveland open cup.

#### USES

The largest uses of monocyclic terpene mixtures are as solvents. One large use is in rubber reclaiming where they serve to swell the scrap rubber. Their ability to dissolve rubber renders them useful in making rubber-based solvent cements (adhesives). Mixed terpenes are used as solvents for paints, varnishes, and other protective coatings. They are higher boiling and have lower aniline points than turpentine. In oleoresinous finishes they function as antiskinning agents.

In general, dipentene can be used where terpene mixtures are satisfactory. It is usually a more desirable raw material than the less pure terpene mixtures for making sulfurized extreme-pressure lubricating-oil additives and synthetic resins. It is a logical starting material for chemical synthesis of isoprene, *p*-cymene, *p*-menthane, and carvomenthene. Both dipentene and carvomenthene can be used for alkylation of phenols by ionic catalysts. The molecular weights of the products from diolefins

are higher than expected because of dimerization through one of the terpene double bonds. Terpene-phenol resins so prepared (or more often from bicyclic terpenes, chiefly pinene) are used in printing inks, adhesives, and protective coatings. The products from dipentene or mixed monocyclics with phenol are antioxidants for rubber.

*p*-Menthane is a raw material for conversion to *p*-menthane hydroperoxide, the chief initiator used in making the so-called "cold" rubber (10), prepared at 5°C. See Vol. 11, pp. 832-33.

*p*-Cymene is used as a raw material for preparing *p*-cymene hydroperoxide, which in turn may be converted to *p*-cresol. It can, like *p*-xylene, be oxidized to terephthalic acid.

Mixtures of monocyclic terpenes are treated with maleic anhydride to prepare dibasic acids which are used in the preparation of alkyl resins for protective coatings (see Vol. 1, p. 527).

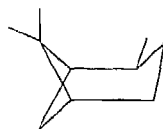
Orange oil (principally *dextro*-limonene) is used as a flavoring material in beverages, pharmaceuticals, extracts, and food.

*Terebene*, a mixture of terpenes containing chiefly dipentene and terpinenes, is used as an expectorant (see Vol. 5, p. 684).

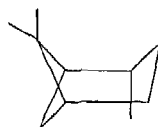
### Bicyclic and Tricyclic Hydrocarbons

The bicyclic terpenes are the most important class of terpenes from a commercial viewpoint. Tricyclic terpenes are of minor importance as such but are present as components of commercial terpene mixtures.

The bicyclic and tricyclic terpenes contain two and three rings respectively. Like the monocyclic terpenes many bicyclic terpenes, for example, pinane, exist in *cis* and *trans* forms (as well as optically active forms):



*cis*-pinane



*trans*-pinane

Their close structural relationship to the monocyclic and acyclic terpenes is illustrated by the fact that thermal rearrangement of  $\alpha$ -pinene, a bicyclic terpene, forms dipentene, a monocyclic terpene, and allo-ocimene, an acyclic terpene. The bicyclic terpenes are designated by trivial names; however, a more systematic system has been proposed (8). The skeleton formulas of the principal bicyclic and tricyclic terpenes are given in Figure 2.

### PHYSICAL AND CHEMICAL PROPERTIES

The determination of the physical properties of the bicyclic and tricyclic terpenes is subject to the difficulties previously described for the monocyclic terpenes. See Table V (21).

The reactivity of bicyclic terpenes is qualitatively similar to that of the monocyclic terpenes. They are unique, however, in their tendency in the presence of a

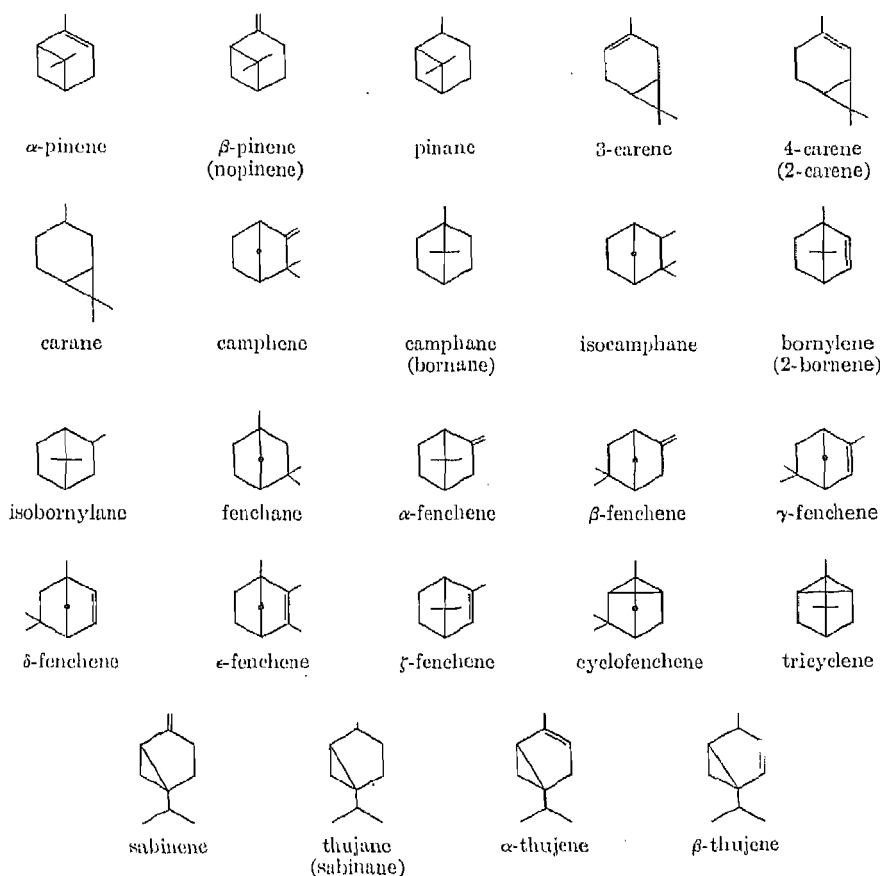


Figure 2.

TABLE V. Physical Properties of Bicyclic Terpenes.

Compound	B.p., °C.		M.p., °C.	$n_D^{20}$	$d_4^{20}$
	760 mm.	100 mm.			
α-Pinene	156 <sup>a</sup>	89	—	1.4658 <sup>a</sup>	0.8595 <sup>a</sup>
β-Pinene	165 <sup>a</sup>	98 <sup>a</sup>	—	1.4790 <sup>a</sup>	0.8722 <sup>a</sup>
cis-Pinane	168 <sup>a</sup>	101 <sup>a</sup>	—	1.4628 <sup>a</sup>	0.8576 <sup>a</sup>
3-Carene	170	104 <sup>a</sup>	—	1.4730 <sup>a</sup>	0.8617
Camphene	158 <sup>a</sup>	91 <sup>a</sup>	49 <sup>a</sup>	1.4695 <sup>25</sup>	0.8675 <sup>25</sup>
Camphane	158 <sup>a</sup>	—	154	—	—
Isocamphane	166 <sup>a</sup>	100 <sup>a</sup>	65 <sup>a</sup>	—	—
Bornylene	146	—	113 <sup>a</sup>	—	—
α-Fenchene	157 <sup>a</sup>	91.5 <sup>a</sup>	—	1.4692 <sup>30</sup>	—
β-Fenchene	151	—	—	1.4645 <sup>18, 30a</sup>	0.8591
γ-Fenchene	146	—	—	1.4607	0.8547
δ-Fenchene	139	—	—	1.4494	0.8381
ε-Fenchene	152	—	—	—	—
ζ-Fenchene	146.5	—	—	1.4685	0.8626
Cyclofenchene	143 <sup>a</sup>	78 <sup>a</sup>	—	1.4459 <sup>30</sup>	0.8595
Tricyclene	152 <sup>a</sup>	106.5 <sup>200a</sup>	65 <sup>a</sup>	1.4625	—
Sabinene	—	—	—	1.4636 <sup>25</sup>	0.8358 <sup>25</sup>
α-Thujene	—	—	—	1.4493 <sup>25</sup>	0.8261 <sup>25</sup>

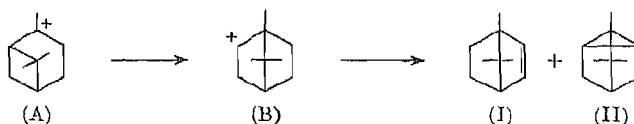
<sup>a</sup> Values from the Laboratories of Hercules Powder Co.

wide variety of acidic materials to form monocyclic terpenes and to rearrange into bicyclic terpenes having a different ring system. A typical example is the conversion of  $\alpha$ -pinene to camphene and a host of other bicyclic and monocyclic terpenes by acid clays, titanate acid, silicic acids, vanadic acids, molybdic acid, silicotungstic acids, and acid magnesium phosphates (2). The reactions are illustrated below using the generally accepted carbonium ion mechanism.

Addition of  $H^+$  from an acid to  $\alpha$ -pinene yields the tertiary carbonium ion (A):



Migration of one bond attached to the bridgehead carbon leads to carbonium ion (B) and then to bornylene (I) and tricyclene (II):



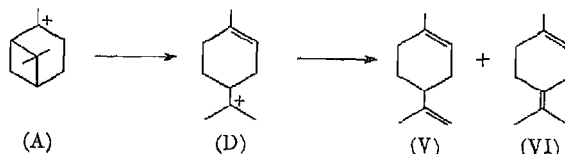
Carbonium ion (B) can rearrange to (C), the precursor of camphene (III):



Migration of the other bond of (A) attached to the bridgehead carbon adjacent to the carbonium carbon leads to  $\alpha$ -fenchene (IV) and other fenchenes:



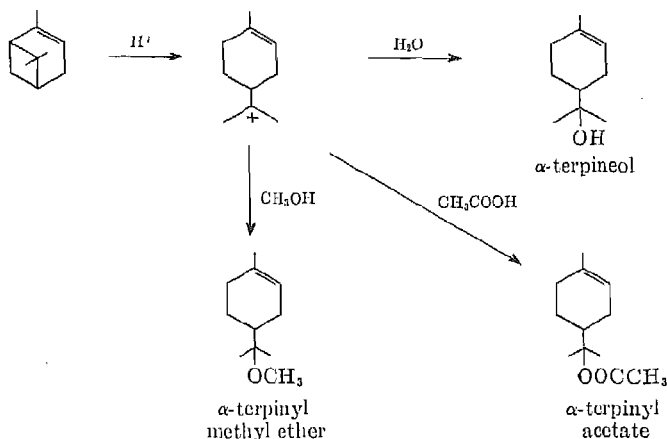
Splitting of the cyclobutane ring in (A) by an acid-catalyzed  $\beta$ -fission reaction leads to dipentene (V), terpinolene (VI), and rearranged terpenes:



If the cyclobutane ring of  $\alpha$ -pinene is opened by acid reagents in the presence of hydroxyl compounds, such as water, acetic acid, or methanol, compounds are formed that correspond to addition of the hydroxyl hydrogen and the remaining fragment of the compound across a double bond of the resulting monocyclic terpene (see Scheme 1).



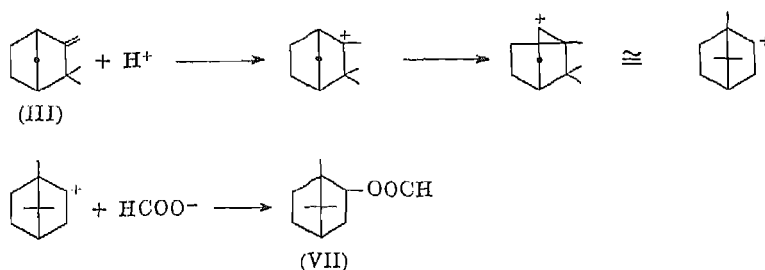
SCHEME 1



The cyclobutane ring in  $\alpha$ -pinene is also opened thermally, presumably by a free-radical mechanism, to yield dipentene and open-chain terpenes (see p. 713).

$\beta$ -Pinene, the more reactive pinene, will undergo most of the reactions of  $\alpha$ -pinene. In addition, it can be polymerized by Friedel-Crafts catalysts to higher-molecular-weight polymers than can  $\alpha$ -pinene and in better yield.

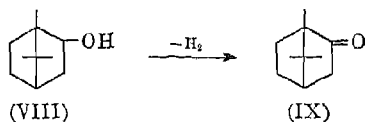
Camphene, like  $\beta$ -pinene, has an exocyclic double bond which is also a vinylidene double bond. Camphene (III) readily adds acids to form isborneol esters like (VII)



The reaction with formic acid to form isbornyl formate (VII) is a convenient route to production of isborneol (VIII):



The dehydrogenation of isborneol is a method for the production of synthetic camphor (IX) (4) (see also Vol. 2, p. 808):



A more complete treatment of the chemical properties of bicyclic terpenes is given by Simonsen (20) and Radt (19).

## OCCURRENCE

The chief sources of bicyclic terpenes are wood, gum, and sulfate turpentines (see *Turpentine*). Commercial turpentine produced in the United States has  $\alpha$ -pinene as its major component. Wood turpentine, which has been distilled from the crude wood oils extracted from pinewood, contains about 75–80%  $\alpha$ -pinene and lesser amounts of fenchenes, camphene, and monocyclic terpenes. Sulfate and gum turpentine contain less fenchene and camphene, but on the order of 25–30%  $\beta$ -pinene depending on the source.

Many turpentines including Indian turpentine from *Pinus longifolia* Roxb. and turpentine from the Western Ponderosa pine have either 3- or 4-carene as their chief component rather than pinenes.

## MANUFACTURE

The bicyclic terpenes which occur naturally are generally separated by fractional distillation to produce the materials of commerce.  $\alpha$ -Pinene is isolated from wood or sulfate turpentine in 85–95% purity by fractional distillation.  $\beta$ -Pinene is isolated from sulfate turpentine commercially in about 80% purity by fractional distillation.

The  $\alpha$ -pinene so isolated is isomerized to **camphene** by the use of acidic materials such as acid clays. The isomerizate, after removal of the catalyst, is fractionally distilled to separate the monocyclic terpenes and concentrate the camphene to the desired degree. Tricyclene (II), a major by-product, need not be removed for the manufacture of isoborneol since it reacts in the same fashion as camphene (2). The presence of fenchenes in commercial camphene is frequently objectionable since they lower the melting point of the camphene and many of its reaction products. When present in camphene used to manufacture camphor, they have been reported to form fenchone. Fenchone, a liquid, depresses the melting point of the camphor (2).

## ANALYSIS

The methods of analysis which have been described for monocyclic terpenes are in general applicable to bicyclic terpenes. The latter are characterized for commercial purposes chiefly by physical constants. When knowledge of the chemical composition is needed, infrared spectroscopy, either alone or after fractional distillation, is employed. Ultraviolet absorption analysis is not generally useful since the common bicyclic

TABLE VI. Physical Properties of Typical Commercial Bicyclic Terpenes.

Property	Wood $\alpha$ -pinene		Sulfate $\alpha$ -pinene		$\beta$ -Pinene		Camphene
	A	B	A	B	A	B	
$d_{15.6}^{15.6}$	0.8634	0.863	0.8630	0.8638	0.873	0.872	0.876
$n_D^{20}$	1.4665	1.466	1.4655	1.4666	1.4755	1.4768	—
Unpolymerized residue, %	0.8	0.4	0.4	0.4	—	—	—
Flash point, °F.	90.5 <sup>a</sup>	98 <sup>b</sup>	98 <sup>b</sup>	—	115	—	—
Kauri-butanol value	52	53	—	—	—	—	—
Distillation range, °C.							
5%	156.3	156.3	156.2	156.6	165.0	164.4	157.0
50%	157.0	156.6	156.3	157.0	165.8	—	158.0
95%	158.3	157.0	156.7	157.9	167.7	167.8	159.0

<sup>a</sup> Cleveland open cup.

<sup>b</sup> Tag open cup.

terpenes contain only one double bond which does not absorb in the ultraviolet region.

*Typical Analyses.* The physical properties of several commercial bicyclic terpenes are given in Table VI.

The chemical analyses of several commercial bicyclic terpene mixtures are given in Table VII.

TABLE VII. Percentage Composition of Typical Commercial Bicyclic Terpenes.

Component	Sulfate $\alpha$ -pinene	Wood $\alpha$ -pinene	Sulfate turpentine	Sulfate $\beta$ -pinene
$\alpha$ -Pinene	94.1	91	62	9.9
$\beta$ -Pinene	1.3	—	22	79.7
Camphene	1.1	6.1	—	0.5
Tricyclene	1.6	1.2	—	—
$\alpha$ -Fenchene	—	1.3	—	—
Dipentene	—	—	—	2.1
Monocyclics	—	—	11	—
Benzaldehyde	0.1	—	—	—
Loss, residue, and unidentified	—	—	3	4.4

#### USES

The largest use of bicyclic terpenes is as solvents. In this application purity is not as critical as for chemical synthesis. Generally wood or gum turpentine is used. Sulfate turpentine is less desirable unless treated to reduce the odor caused by sulfur-containing impurities. Much of the turpentine used in the formulation of paints has been displaced by petroleum solvents, but turpentine is still the chief solvent for "over-the-counter" sales to the ultimate consumer for thinning paints and brush cleaning.

$\alpha$ -Pinene is widely used as a chemical intermediate for the synthesis of synthetic pine oil, terpin hydrate, camphene, terpineol ethers, terpene-phenol resins (see p. 726), and reaction products with phosphorus sulfides for use as oil additives.

Camphene is used as a raw material for insecticides (Thanite (isobornyl thiocyanacetate) and toxaphene (chlorinated camphene)), isoborneol, isobornyl acetate, and camphor.

$\beta$ -Pinene is used primarily to produce synthetic resins by acid polymerization (see *Terpene resins*).

#### Cyclic Alcohols

The cyclic terpene alcohols as individual compounds or mixtures such as pine oil rank as the most important derivatives of the cyclic terpene hydrocarbons.

Since there are relatively few commercially important cyclic terpene alcohols, the monocyclic and bicyclic terpene alcohols will be treated together. These alcohols can be designated by systematic names, but trivial names are generally used for the more common alcohols. The monocyclic terpene alcohols can be named as derivatives of *p*-menthane (that is, menthans, menthenols, and menthadienols) using the numbering scheme given (p. 720). The bicyclic terpene alcohols can be named by the accepted rules for nomenclature of bicyclic derivatives. The structures of the more common terpene alcohols with their common names are given in Figure 3.

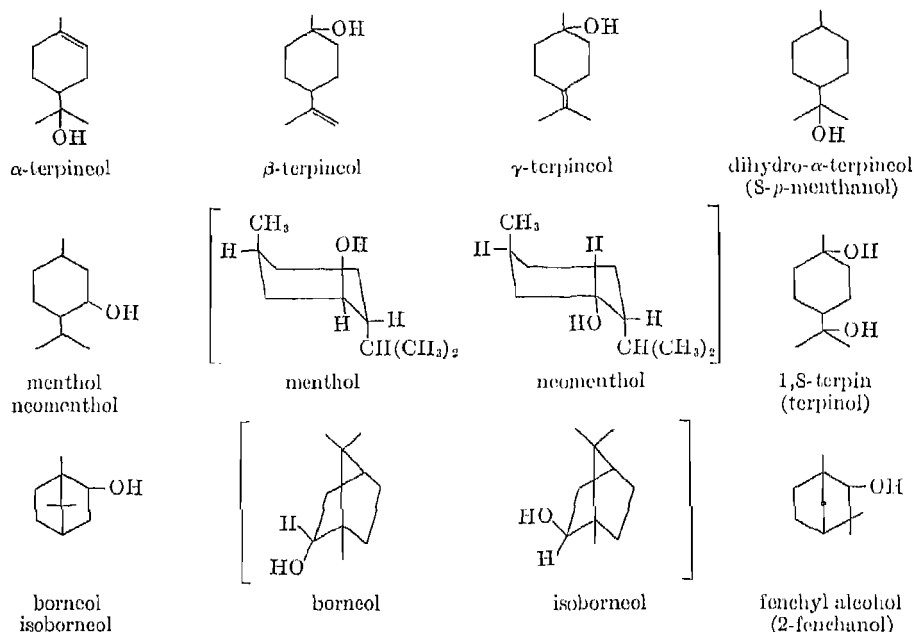


Figure 3.

## PHYSICAL AND CHEMICAL PROPERTIES

The physical properties are listed in Table VIII.

TABLE VIII. Physical Properties of Cyclic Terpene Alcohols.

Compound	B.p., C°.		M.p., °C.	$n_D^{20}$	$d_4^{20}$
	760 mm.	100 mm.			
α-Terpineol	219	149 <sup>a</sup>	36 <sup>a</sup>	1.4831 <sup>a</sup>	0.9336
β-Terpineol	209	139 <sup>a</sup>	33	1.4712 <sup>30</sup>	0.919
γ-Terpineol	218	132 <sup>50a</sup>	68 <sup>a</sup>	1.4912	0.9412
Menthol	217	—	38	1.4615	0.8911 <sup>30</sup>
<i>cis</i> -1,8-Terpin	258	—	105	—	—
<i>cis</i> -1,8-Terpin hydrate	—	—	117	—	—
<i>cis</i> -8- <i>p</i> -Menthanol	210	124.5 <sup>60a</sup>	45 <sup>a</sup>	1.4665	—
<i>trans</i> -8- <i>p</i> -Menthanol	209	122.5 <sup>60a</sup>	34 <sup>a</sup>	1.4630	—
Borneol	212	—	210 ( <i>dl</i> )	—	1.01
Isoborneol	214 Subl.	—	212 ( <i>dl</i> )	—	—
α-Fenchyl alcohol	201	133 <sup>a</sup>	39 <sup>a</sup>	1.4734 <sup>a</sup>	0.935 <sup>40</sup>
β-Fenchyl alcohol	201	73 <sub>7.5</sub>	6	1.4766	—

<sup>a</sup> Values from the Laboratories of Hercules Powder Co.

The cyclic terpene alcohols with heat or catalysts or both dehydrate to terpene hydrocarbons. The tertiary alcohols in general dehydrate more readily than the secondary alcohols. Isoborneol dehydrates more readily than borneol, but both yield camphene. The remaining alcohols dehydrate to a mixture of olefins. Cracking of the methylxanthate (the Chugaev reaction) is a more desirable laboratory method when individual products are desired since it ordinarily gives no rearranged olefins.

With mild dehydrating agents 1,8-terpin can be partially dehydrated to a mixture of terpineols.

The alcohols can be treated with several organic acids and anhydrides to form esters. The reaction is accompanied by dehydration in the case of the tertiary alcohols. Some of these esters, such as the acid phthalates, are used to identify the secondary alcohols such as borneol and menthol.

The secondary alcohols can in general be oxidized with nitric or chromic acid, or dehydrogenated to ketones (3). Thus isoborneol and borneol can be converted to camphor. More drastic oxidation of borneol, isoborneol, or camphor with nitric acid using a mercury catalyst (25) yields camphoric acid.

#### OCCURRENCE

The chief commercial source of the cyclic alcohols in nature is the extract from southern pine stumps. These alcohols are presumably formed by hydration of terpene hydrocarbons in the stump. The chief alcohol present is  $\alpha$ -terpineol with lesser amounts of 1,8-terpin, fenchyl alcohol, dihydro- $\alpha$ -terpineol, and borneol. The mixture of terpene alcohols exclusive of terpin is usually designated *pine oil*.

*levo*-Menthol occurs in American, Chinese, Japanese, and other oils of peppermint and mint, which are obtained from the leaves of the *Mentha* species (see Vol. 9, pp. 584, 587; ref. 9, Vol. III, pp. 586, 640).

#### MANUFACTURE

A mixture of the tertiary cyclic alcohols containing some borneol, fenchyl alcohol, estragole (*p*-allylanisole), and fenchone is isolated as **pine oil** by fractional distillation of the volatile fraction of crude oils extracted from pine stumps. A more efficient distillation yields commercial  $\alpha$ -**terpineol** which contains 95% of tertiary alcohols, chiefly  $\alpha$ -terpineol. In the distillation of the alcohols to obtain  $\alpha$ -terpineol, a fraction rich in secondary bicyclic alcohols is obtained but this fraction is usually not separated into specific compounds. The commercial pine oils are thus prepared by varying degrees of fractional distillation and blending to meet specific needs. The U.S. production of pine oil for the naval stores crop year April 1952 to March 1953 was 7,280,000 gal. (15).

The hydration of  $\alpha$ -pinene with sulfuric acid, water, and acetone yields synthetic pine oil, which is chiefly  $\alpha$ -terpineol. By-products include monocyclic terpenes and cineoles.

Dehydration of 1,8-terpin with acid catalysts such as phosphoric acid or oxalic acid yields a mixture of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -terpineols known as **terpineol extra** or **prime terpineol**. These terpineols are superior to the natural product in cases where a pleasant odor is desired (see Vol. 10, p. 18). The  $\beta$ - and  $\gamma$ -terpineols are not isolated commercially. The production of terpineols, not including pine oil, was 2,013,000 lb. in 1953. The unit value was \$0.20 per pound.

The dihydroterpineols can be readily prepared by catalytic hydrogenation of the terpineols, but the reaction is not carried out commercially.

***cis*-1,8-Terpin hydrate** is isolated from pinewood crude oils by steaming the residual rosin after distillation of the more volatile terpenes and is further purified by recrystallization. It is produced synthetically by the hydration of  $\alpha$ -pinene with sulfuric acid and water.

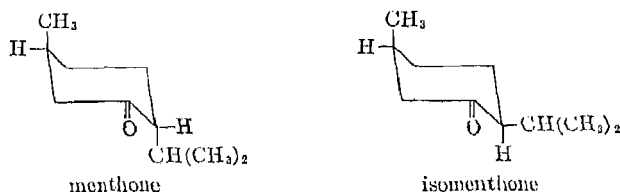
Destructively distilled pine oil is prepared by fractional distillation of the volatile oils produced by the destructive distillation of pinewood.

*levo*-Menthol is isolated from peppermint oil, obtained from the peppermint plant by steam distillation. The plant may be partially dried to reduce its weight and to reduce steam requirements. The oil so obtained may be again steam-distilled or fractionally distilled dry under vacuum to concentrate the menthol. The product is chilled to cause crystallization of the menthol (12,16). The menthol is removed by filtration or centrifugation.

*levo*-Menthol can be synthesized from *dextro*-citronellal (see p. 718), which is obtained from oil of citronella. The *dextro*-citronellal is cyclized to isopulegols (8-*p*-menthen-3-ol stereoisomers), which are hydrogenated to menthols, predominately *levo*-menthol. It is isolated by crystallization of its esters and hydrolysis. The odor of synthetic menthol has been improved by spraying with mint oil or by recrystallization from the by-product terpenes obtained in the distillation or crystallization of peppermint oils.

In addition to *levo*-menthol, *dl*-menthol is accepted by the U.S.P. This menthol, together with other optical and *cis* and *trans* isomers, is obtained by reduction of thymol or certain of the monocyclic terpene ketones (such as pulegone and piperitone) which have the keto group in the 3-position. Isolation of the *dl*-menthol is carried out by recrystallization of the acetates or oxalates.

A more feasible process (1) involves hydrogenation of thymol to a mixture of *dl*-menthone, *dl*-isomenthone, and the corresponding alcohols. By refluxing this mixture in the presence of a dehydrogenation catalyst (copper chromite) and an enolization catalyst (sodium hydroxide) an equilibrium mixture of *dl*-menthone and *dl*-isomenthone is obtained.



If an efficient distillation column is used to remove the lower-boiling menthone as it is formed, the major part of the reaction mixture can be converted to this isomer. Catalytic hydrogenation of menthone yields *dl*-neomenthol and *dl*-menthol. The *dl*-menthol is crystallized from the mixture and the *dl*-neomenthol is recycled to the dehydrogenation step.

The production and sales of synthetic menthol in 1952 are given in Table IX (data from U.S. Tariff Commission Reports). In 1953 the total sold was 255,000 lb. at a unit value of \$4.46.

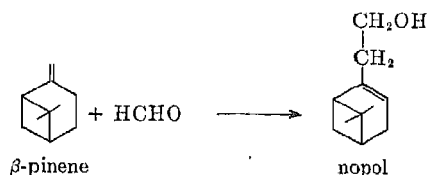
The only secondary cyclic terpene alcohol which is produced in large volume is

TABLE IX. Production and Sales of Synthetic Menthol in 1952.

	Production, 1,000-lb. units	Sales		
		Quantity, 1,000 lb.	Value, \$1,000	Unit value
Total	390	277	1,394	5.03
Technical	148	68	291	4.26
U.S.P.	242	209	1,103	5.27

**isoborneol.** This alcohol is produced as an intermediate in the camphor process by reaction of camphene with formic acid and hydrolysis of the resulting isobornyl formate.

A primary alcohol related to the bicyclic terpenes is **nopol** (24). This derivative is prepared by the reaction of formaldehyde with  $\beta$ -pinene.



#### ANALYSIS

Cyclic terpene alcohols are characterized by physical constants such as specific gravity, refractive index, color, flash point, freezing point, distillation range, viscosity, and aniline point (lowest temperature of miscibility with an equal volume of aniline). They are further characterized according to composition by the content of moisture, tertiary alcohols, total alcohols, and  $\alpha$ -terpineol. The  $\alpha$ -terpineol content is best determined by infrared absorption. The content of anethole and estragole in pine oil can be determined by ultraviolet absorption.

Analytical fractional distillation can be used on cyclic terpene alcohols, but care must be exercised to avoid dehydration from overheating or the presence of acidic substances. If borneol is present in significant amounts, it will cause plugging of the column, because of its high melting point.

Prime terpeneol can be separated into a  $\beta$ -terpineol fraction and an  $\alpha$ - and  $\gamma$ -terpineol mixture by distillation in a column of sixty or more theoretical plates.

*Typical Analyses.* Physical properties of several commercial terpene alcohol mixtures are given in Table X. A typical commercial terpin hydrate has the analysis shown in Table XI.

TABLE X. Physical Properties of Typical Commercial Cyclic Terpene Alcohols.

Property	Pine oil				$\alpha$ -Terpineol	Prime terpeneol
	A	B	C	D		
$d_{40}^{20}$	0.931	0.9442	0.938	0.944	0.9415	0.9394
$n_D^{20}$	1.4808	1.4820	1.4822	1.483	1.4840	1.4825
Flash point, °F.	167	188	—	190	194	190
Freezing point, °F.	—	47	—	—	81.5	< +14
Total alcohols, %	—	89	77	87	97	96.5
Distillation range, °C.						
5%	194.6	214.4	205	214	219	—
50%	211.4	216.6	210	—	220	218.5
95%	221.5	218.7	217	220	222	219.7

TABLE XI. Analysis of Commercial Terpin Hydrate.

Terpin hydrate content, %	99
M.p. (capillary), °C.	118
Moisture	None
Ash	Trace (less than 0.09%)
Oils	Trace (less than 0.50%)

A good grade of natural pine oil will have a composition similar to:

Component	Amount, %
$\alpha$ -Terpineol	65-70
Dihydro- $\alpha$ -terpineol and other tertiary alcohols	10
Borneol and fenchyl alcohol	10-15
Estragole	5
Ketones	5-10

Commercial  $\alpha$ -terpineol has had the major portion of the secondary alcohols and ketones removed and contains 95% or more of tertiary alcohols.

The prime terpineols obtained from dehydration of terpin hydrate differ from that of natural origin in that they contain significant amounts of  $\beta$ - and  $\gamma$ -terpineols. The analysis of a terpineol of this type is:

Component	Amount, %
$\alpha$ -Terpineol	58
$\beta$ -Terpineol	18
$\gamma$ -Terpineol	15
Cineoles and hydrocarbons	4

#### USES

Pine oil is widely used as a frother in the separation of minerals by flotation (*q.v.*). The textile industry uses it as a penetrant, dispersing agent, wetting agent, and inhibitor of bacterial growth in practically all wet-processing of cotton, silk, rayon, and woolen goods, including scouring, bleaching, desizing, fulling, degumming, dyeing, and printing (see *Textile technology*). Pine oil is used as a solvent and bactericide in soaps and other disinfecting compounds. It is used as a solvent for chlorinated phenols in the treatment of lumber and as a preservative for casein and other proteins in adhesives and water paints.

Menthol (U.S.P. XIV) is used externally to relieve pain as in toothache and sore throat. It is used internally as an anodyne, anesthetic, and antispasmodic. It is also used to produce "coolness" in cigarettes. See *Flavors and spices; Perfumes (synthetic and isolates)*.

Fenchyl alcohol and borneol are not used in significant quantities commercially. Isobornyl acetate, a synthetic product, is used in perfumes. *cis*-1,8-Terpin hydrate is used in medicinal preparations as an expectorant (see Vol. 5, p. 684). It also serves as a raw material for dehydration to prime terpineol. Nopol is a relatively new product which has found use in several applications, such as perfumery, wetting agents, and resins.  $\alpha$ -Terpineol is used in the preparation of terpinyl acetate for the essential oil manufacturers and in other applications where a product of higher purity than pine oil is required.

#### Cyclic Ketones

The cyclic terpene aldehydes (see Vol. 10, p. 21), unlike some of the acyclic terpene aldehydes, are not important articles of commerce, and the cyclic terpene ketones, with the exception of camphor (*q.v.*), are only slightly more so.



The cyclic terpene ketones are named chiefly by trivial names. A representative group of monocyclic and bicyclic terpene ketones is given in Figure 4.

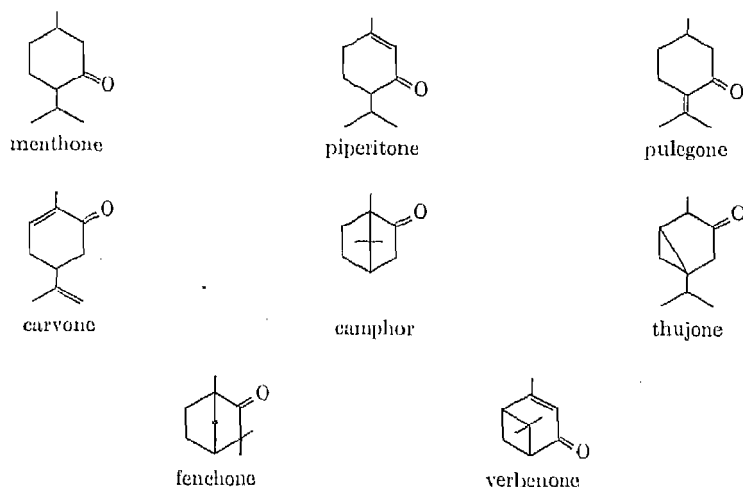


Figure 4.

#### PHYSICAL AND CHEMICAL PROPERTIES

The physical properties of several selected cyclic terpene ketones are given in Table XII.

TABLE XII. Physical Properties of the Principal Cyclic Terpene Ketones.

Compound	B.p., °C.		M.p., °C.	$n_D^{20}$	$d_4^{20}$
	760 mm.	100 mm.			
Menthone	210	119 <sub>60</sub>	-6	1.4500 <sup>a</sup>	0.8946
Piperitone	233-35	—	—	1.4845	0.9324
Pulegone	221-23	—	—	1.4849	0.9401 <sub>20</sub>
Carvone	230	—	—	1.4995	—
Thujone	200	—	—	1.4537	0.9189 <sub>20</sub>
Fenchone	193	122 <sup>a</sup>	6	1.4619 <sup>a</sup>	0.9452
Verbenone	—	—	10	1.4965	0.9754
Camphor	—	—	179	—	1.0000 <sup>a</sup>

<sup>a</sup> Values from the Laboratories of Hercules Powder Co.

The reactions of cyclic terpene ketones are largely those characteristic of simple ketones. The reactivity and products formed in such reactions as oxidation and halogenation are of course affected by the substituents on the  $\alpha$ -carbon. These ketones are in general reduced to alcohols and hydrocarbons and oxidized to acids. They form oximes, hydrazones, and semicarbazones. The only reactions that have assumed commercial importance are the oxidation of camphor to camphoric acid and the reduction of ketones such as pulegone and piperitone to synthetic menthol.

#### OCCURRENCE

Fenchone occurs as a minor component of pinewood oils. Its boiling point is between that of the monocyclic terpenes and the secondary terpene alcohols. It

forms an azeotrope with terpinolene and is thus concentrated in the high-boiling fraction of monocyclic terpenes.

*levo*-Menthone occurs in peppermint and pennyroyal oils. Thujone occurs in oil of thuja and sage. *dextro*-Carvone occurs in caraway and dill seed oils. *levo*-Carvone is the principal constituent of spearmint oil. *dextro*-Piperitone is found in oil of *Andropogon invarancusa* Jones. Pulegone is the principal constituent of pennyroyal oil. Further details on the occurrence of terpenes in essential oils are given by Guenther (9).

#### MANUFACTURE

**Camphor** is produced by oxidation of isoborneol obtained from camphene. Chemical oxidants can be used but catalytic dehydrogenation is preferred (4). See Vol. 3, p. 812.

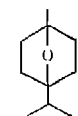
**Fenchone** can be produced from the volatile oils extracted from southern pine stumps. Its boiling point of 193°C. is between that of terpinolene (186°C.) and  $\alpha$ -fenchyl alcohol (201°C.). It is usually found in both the monocyclic fraction and pine oil fraction and can be concentrated by fractional distillation.

#### USES

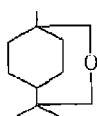
Fenchone is used as a solvent for vinyl resin finishes and as a pine scent. The remaining ketones described are used in the perfumery and essential oil trade.

#### Cyclic Ethers and Peroxides

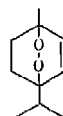
The important terpene ethers and peroxides are 1,4-cineole, 1,8-cineole (eucalyptole, U.S.P. XIV), and ascaridole.



1,4-cineole



1,8-cineole



ascaridole

#### PHYSICAL AND CHEMICAL PROPERTIES

The physical properties of the two cineoles and ascaridole are given in Table XIII.

TABLE XIII. Physical Properties of the Cineoles and Ascaridole.

Compound	B.p., °C.		M.p., °C.	$n_D^{20}$	$d_4^{20}$
	760 mm.	100 mm.			
1,4-Cineole	172	105.5 <sup>a</sup>	-46	1.4446 <sup>a</sup>	0.8086 <sup>a</sup>
1,8-Cineole	174	108 <sup>a</sup>	1	1.4574 <sup>a</sup>	0.9245 <sup>a</sup>
Ascaridole	—	113-4 <sub>20</sub>	2	—	1.0114 <sub>18</sub> <sup>18</sup>

<sup>a</sup> Values from the Laboratories of Hercules Powder Co.

The notable feature of 1,8-cineole is the ease with which it forms complexes with materials that can coordinate with a pair of electrons on the oxygen bridge. Thus it forms complexes with resorcinol, 1-naphthol, hydrogen chloride, and phosphoric acid. The formation of these complexes can serve as a method of isolation.

In contrast to 1,8-cineole, 1,4-cineole does not form complexes of this type. The reaction with hydrogen bromide to form terpinene hydrobromide, elementary analysis,

and oxidation with potassium permanganate to a slightly soluble acid melting at 157°C. have served to identify 1,4-cineole. Infrared absorption is a more convenient method of analysis.

Ascaridole is a relatively unstable peroxide which decomposes violently when heated to 130–50°C. Complete hydrogenation with palladium catalyst yields 1,4-*p*-menthanediol. Hydrogenation of only the double bond of ascaridole with platinum oxide catalyst forms dihydroascaridole, which has much greater stability than the unsaturated peroxide or in fact most peroxides (*q.v.*). Thus heating for 18 hours at 140°C. caused no decomposition (14). This difference is apparently caused by the double bond in the unhydrogenated ascaridole which tends to pull the ring into a planar position causing a strain in the peroxide bond.

#### OCCURRENCE

1,8-Cineole occurs widely in nature in essential oils including leaf oil of *Litsea guatemalensis* (49.6%), Mysore cardamom oil (80%), *Blumea lacera* leaf oil (66%), Spanish sage, laurel leaf oil (50%), and cajuput oil (40%). The major commercial source is the oil from various species of *Eucalyptus*.

1,4-Cineole seems to be much less widely distributed but has been identified in several essential oils including mullilam oil and cubeb oil. The fact that 1,4-cineole is less readily identified than 1,8-cineole may partly explain why it has been found less frequently.

Ascaridole is the major component of chenopodium oil (American wormseed oil). Since ascaridole can be prepared from  $\alpha$ -terpinene and oxygen in the presence of ultra-violet light and chlorophyll, it has been postulated that this is the method of synthesis in plants.

#### MANUFACTURE

**Cineoles** are not synthesized intentionally on a commercial scale but are produced as by-products together with monocyclic terpenes from reactions such as the dehydration of terpin to terpineols and the hydration of pinene to synthetic pine oil. They are not isolated from these mixtures with monocyclic terpenes. Cineoles can be prepared in about 40% yield by steam distillation of 1,8-terpin hydrate with 8% phosphoric acid. Other mild dehydration conditions can also be used. 1,8-Cineole is isolated from various *Eucalyptus* oils by chilling to effect crystallization. The production in 1952 was 23,000 lb. and the unit value was \$1.54 per pound.

#### USES

1,8-Cineole (eucalyptole) is an expectorant and antiseptic (see Vol. 5, p. 681). It is used in nose and throat sprays.

Ascaridole has been used as an anthelmintic against hookworm and other nematodes and cestodes but is dangerous because of its toxicity (see Vol. 1, p. 939).

#### Bibliography

- (1) Barney, A. L., and Hass, H. B., *Ind. Eng. Chem.*, **36**, 85 (1944).
- (1a) Barton, D. H. R., and Harper, S. H. R., in Rodd, *Chemistry of Carbon Compounds*, Elsevier, Houston, Tex., 1953, Vol. IIB, chs. XII–XVI.
- (2) Coates, W. M., *Perfumery Essent. Oil Record*, **43**, No. 9, 930 (1952).
- (3) Coates, W. M., *Perfumery Essent. Oil Record*, **43**, No. 10, 360 (1952).

- (4) Colborne, R. S., and Huggett, W. E., B.I.O.S. Trip, No. 2179, B.I.O.S. PB Rept. 87341.
- (5) Crosby Chemicals, *Crosby Products*, DeRidder, La.
- (6) Davenport, J. B., Sutherland, M. D., and West, T. F., *J. Appl. Chem.*, **1**, 527 (1951).
- (7) Delta Pine Products Corporation, *Product Data Sheets*, Covington, La.
- (8) Graffin, M. W., *Chem. Eng. News*, **32**, 1795 (1954).
- (9) Guenther, E. *et al.*, *The Essential Oils*, Van Nostrand, N.Y., 1947-52, Vols. I-VI.
- (10) Hercules Powder Co., *Hercules Hydroperoxides* (Tech. Service Bull. No. 177), Wilmington, Del., 1953.
- (11) Hercules Powder Co., *Terpenes and Related Materials*, Wilmington, Del., 1951.
- (12) Jacobs, M. B., *Am. Perfumes*, **48**, No. 10, 64 (1946).
- (13) Kesterson, J. W., and McDuff, O. R., *Univ. Florida, Agr. Expt. Sta. Bull.* (1948).
- (14) Moore, C. G., *J. Chem. Soc.*, **1951**, 234.
- (15) *Naval Stores Review, International Yearbook*, H. L. Peace Publications, New Orleans, La., 1953.
- (16) Naves, Y. R., *Mfg. Chemist*, **17**, 525 (1946).
- (17) Newport Industries, *Newport Products*, N.Y., 1952.
- (18) *Oil, Paint Drug Repr.*, various dates.
- (19) Radt, F. (ed.), *Elsevier's Encyclopaedia of Organic Chemistry*, Elsevier, Houston, Tex., and Amsterdam, Vol. 12A, 1948.
- (20) Simonsen, J. L., and Owen, L. N., *The Terpenes*, 2nd ed., University Press, Cambridge, England, 1947, 1949, Vols. I and II.
- (21) Sutherland, M. D., *Univ. Queensland Papers, Dept. Chem.*, **1**, No. 34 (1948).
- (22) Sutherland, M. D., and Contes, W. M., *Perfumery Essent. Oil Record*, **43**, No. 12, 453 (1952).
- (23) The Glidden Co., Naval Stores Division, *Data Sheets*, Jacksonville, Fla.
- (24) The Glidden Co., *Nopol*, Jacksonville, Fla., 1951.
- (25) U.S. Pat. 2,333,718 (Nov. 9, 1943), P. Heisel

W. S. ROPP

### SESQUITERPENOIDS

The terms sesquiterpene and sesquiterpenoid are applied to compounds the skeleton of which may be considered to be derived from three isoprene units. Many such substances have been so described, but few have been adequately characterized. While such compounds have been known in more or less pure form for over a century, only since 1920 has their chemistry been placed on a more adequate basis.

Sesquiterpenoids are widely distributed in nature (14) and occur in the essential oils of plants, especially the Coniferae and the Rutaceae, in the flowers, fruit, and leaves, and also in the wood and roots or rhizomes. (See also *Oils, essential.*) Some sources and properties of the better-characterized sesquiterpenoids are shown in Table I (the third column gives the number of carbocyclic rings).

The majority of the sesquiterpenoids are liquids or very low-melting solids and frequently occur in admixture with closely related compounds so that numerous sesquiterpenoids recorded in the early literature are mixtures of known compounds that are very difficult to separate. Some of the oxygenated compounds, particularly the lactones such as santonin, are well-defined crystalline solids.

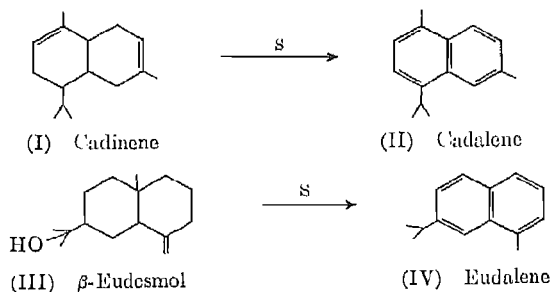
#### THE CARBON SKELETON

The elucidation of the structure of these compounds can be much complicated by rearrangement of the Wagner-Meerwein type (as an example, see "Longifolene," below) or by cyclization (caryophyllene) or cyclopropane ring opening.

Wallach, who made the original suggestion that the sesquiterpenoid skeleton might be built from three isoprene units, viewed these compounds as partially hydrogenated

naphthalene derivatives. However, neither he nor other workers were able to obtain such derivatives by degradation. In fact, until 1920, only the structure of one acyclic alcohol, farnesol, had been elucidated.

In 1921 Ruzicka (26) and his collaborators applied the technique of sulfur dehydrogenation, which Vesterberg had used in his work on abietic acid (see p. 752) to the problems of sesquiterpenoid chemistry. They found that cadinene (I) when so treated gave 1,6-dimethyl-4-isopropyl-naphthalene (cadalene) (II) containing all the original carbon atoms. Later work demonstrated that other sesquiterpenoids yielded naphthalenic hydrocarbons which contained one carbon atom less than the original skeleton: thus eudesmol (a mixture of two isomers,  $\alpha$ - and  $\beta$ -eudesmol (III)) gave eudalene (1-methyl-7-isopropyl-naphthalene) (IV). The eliminated carbon atom (originally, therefore, tertiary) was correctly assumed to be placed in accordance with the isoprene rule.



While many sesquiterpenoids thus lead to naphthalenic residues, others, instead, yield blue azulenic hydrocarbons. These hydrocarbons are themselves found in the higher-boiling fractions of many essential oils, but their interrelation was not possible until the more recent elucidation of the azulene skeleton (1,13,17). On dehydrogenation with sulfur, several sesquiterpenoids (for example, guaialol), yield guaiazulene (*S*-guaiazulene, 1,4-dimethyl-7-isopropylazulene) (V) while others (for example, the vetivones) give vetivazulene (4,8-dimethyl-2-isopropylazulene) (VI). In both of these skeletons the isoprene rule is observed, and the isoprene residues can be regarded as arranged head-to-tail. A complication in such dehydrogenations is that rearrangement can take place. Thus, if selenium is used in the dehydrogenation of guaialol, different azulene, *Se*-guaiazulene, is obtained.



Finally, there are cyclic sesquiterpenoids which do not yield to the dehydrogenative technique. Among these are the compounds cedrene and caryophyllene, the structures of which have recently been established by elegant oxidative degradations.

#### COMMERCIAL ASPECTS

While the essential oils of which the sesquiterpenoids are constituents find application in many fields including medicine, perfumery and soaps, the chemical individuals

TABLE I. Sesquiterpenoids.

Compound	Formula	No. of rings	Typical source	B.p., °C.	$n_D^{25}$	$d_4^{25}$	$[\alpha]_D^{25}$	M.p. of derivative, °C.
Hydrocarbons								
Aromadendrene	$C_{15}H_{24}$	3	Eucalyptus oils	121/10 mm.	1.4978 <sup>20</sup>	0.9116 <sup>20</sup>	-6.5(f)	Aromadendrone, 84.5-85
Bisabolene	$C_{15}H_{24}$	1	Very widely distributed, e.g. in oil of bergamot, bisabol myrrh	134/12 mm.	1.4923 <sup>21</sup>	0.8717 <sup>21</sup>	—	Trihydrochloride, 78-80
Cadinene	$C_{15}H_{24}$	2	Oil of cubebs, oil of cade	136/11 mm.	1.5079 <sup>20</sup>	0.9180 <sup>20</sup>	-125(e)	Dihydrochloride, 117-8
Calamene	$C_{15}H_{24}$	2?	Oil from rhizomes of <i>Acorus calamus</i> L.	126/11 mm.	1.5057 <sup>21</sup>	0.9224 <sup>20</sup>	+5	—
Caryophyllene	$C_{15}H_{24}$	2	Oil of cloves, French lavender oil	125/10 mm.	1.4988 <sup>20</sup>	—	-9	Dihydrochloride, 69-70
$\alpha$ -Cedrene	$C_{15}H_{24}$	3	Cedarwood oil	100/4 mm.	1.4982 <sup>20</sup>	0.9342 <sup>20</sup>	-91	Nitroschloride, 100-2
Copaene	$C_{15}H_{24}$	3	Oil of copaiba, oil of <i>Sin-dora waltichii</i> Benth.	115/10 mm.	1.4887 <sup>25</sup>	0.9555 <sup>25</sup>	$\pm 1$	Cadinene dihydrochloride
$\alpha$ -Costene	$C_{15}H_{24}$	2?	Oil of costus from roots of <i>Saussurea lappa</i>	126/12 mm.	1.4981 <sup>15</sup>	0.9014 <sup>21</sup>	-12	—
$\beta$ -Costene	$C_{15}H_{24}$	1?	Oil of costus from roots of <i>Saussurea lappa</i>	149/18 mm.	1.4905	0.8728 <sup>22</sup>	+6	—
$\alpha$ -Curcumene	$C_{15}H_{22}$	1	Oil from rhizomes of <i>Curcuma aromatica</i> Salisb.	130/13 mm.	1.5001 <sup>25</sup>	0.8775 <sup>20</sup>	-42(e)	Nitrosate, 101
$\beta$ -Curcumene	$C_{15}H_{24}$	1	Oil from rhizomes of <i>Curcuma aromatica</i> Salisb.	142/19 mm.	1.491 <sup>20</sup>	0.8670 <sup>25</sup>	-48(e)	Trihydrobromide, 73-4
$\alpha$ -Gurjunene	$C_{15}H_{24}$	2?	Gurjun balsam	116/10 mm. (128/10 mm.)	1.5010 <sup>20</sup>	0.918 <sup>20</sup>	-180	—
$\beta$ -Gurjunene	$C_{15}H_{24}$	3	Gurjun balsam	123/13 mm.	1.5028	0.9348 <sup>20</sup>	+75	Derived ketone semicarbazone, 243
Humulene ( $\alpha$ -caryophyllene)	$C_{15}H_{24}$	1	Oil of hops	127/12 mm.	1.5021 <sup>13</sup>	0.9001 <sup>15</sup>	—	Nitroschloride, 177
Longifolene	$C_{15}H_{24}$	3	Oleoresin of <i>Pinus longifolia</i> , <i>P. khasya</i>	151/36 mm.	1.4950 <sup>23</sup>	0.9284 <sup>20</sup>	+43	Hydrochloride, 59-60
$\alpha$ -Santalene	$C_{15}H_{24}$	3	East Indian sandalwood oil	117/7 mm.	1.4900 <sup>20</sup>	0.9102 <sup>20</sup>	+2(f)	Nitroschloride, 122
$\beta$ -Santalene	$C_{15}H_{24}$	2	East Indian sandalwood oil	125/7 mm.	1.4941 <sup>20</sup>	0.8940 <sup>20</sup>	-50(f)	Ekasantallic acid, 64
$\beta$ -Selinene	$C_{15}H_{24}$	2	Celery oil	139/17 mm.	1.5031 <sup>20</sup>	0.9107 <sup>20</sup>	+31	Hydrochloride, 72-4
Sesquibienihene	$C_{15}H_{24}$	2	Oil from <i>Chamaecyparis formosensis</i>	130/10 mm.	1.5033 <sup>20</sup>	0.9564 <sup>25</sup>	-4	Dihydrochloride, 103-4

Sesquichamene	$C_{15}H_{24}$	3	Oil from leaves of <i>Chamaecyparis obtusa</i>	123/12 mm.	1.5021 <sup>28</sup>	0.9277 <sup>28</sup>	-90	Nitroschloride, 78-9
Vetivene (mixture)	$C_{15}H_{24}$	2 and 3	Oil of vetiver from <i>Vetivaria zizanioides</i> Stapf	133/12 mm.	1.5179 <sup>15</sup>	0.9339 <sup>15</sup>	—	—
Zingiberene	$C_{15}H_{24}$	1	Oil of ginger	127/12 mm. 134/14 mm.	1.5143 <sup>15</sup> 1.4956 <sup>30</sup>	0.9372 <sup>15</sup> 0.8684 <sup>30</sup>	— -73	Dihydrochloride of isozingiberene, 169-70
Alcohols								
Bulnesol	$C_{15}H_{26}O$	2	Guaiac wood oil	M.p. 69-70 B.p. 138/4 mm.	1.4892 <sup>20</sup>	0.9389 <sup>20</sup>	—	Dihydrobulnesol, 75-6
Cadinol	$C_{15}H_{26}O$	2	Galbanum oil	156/12 mm.	1.5054 <sup>14</sup>	0.9665 <sup>14</sup>	+8	Cadinene hydrochloride Acetate, 85
Calamendiol	$C_{15}H_{26}O_2$	2	Oil from rhizomes of <i>Acorus calamus</i> L.	M.p. 169	—	—	-4(a)	—
Calamenol	$C_{15}H_{24}O$	—	Oil from rhizomes of <i>Acorus calamus</i> L.	150-60/13 mm.	1.5098	0.9612 <sup>20</sup>	—	—
Carotol	$C_{15}H_{26}O$	2	Oil of <i>Daucus carota</i> L.	98/0.3 mm.	1.4997 <sup>30</sup>	0.9702 <sup>30</sup>	+7(a)	Oxide, 118
<i>prim</i> -Cedrenol	$C_{15}H_{24}O$	3	Higher-boiling fractions of cedarwood oil	169/10 mm.	1.5212 <sup>30</sup>	1.0083 <sup>30</sup>	-2 (acetate)	—
Cedrol	$C_{15}H_{26}O$	3	Cedarwood oil	M.p. 86 B.p. 232	—	—	+10(c)	Phenylurethan, 106-7
Costol	$C_{15}H_{26}O$	2	Oil from roots of <i>Saussurea lappa</i>	171/11 mm.	1.5200	0.9803 <sup>21</sup>	+13	Semicarbazone from derived aldehyde, 217-8
Cryptomeradol	$C_{15}H_{26}O$	2?	Japanese cedarwood oil	M.p. 79-80 B.p. 142/4 mm.	1.4932 <sup>30</sup>	0.9515 <sup>60</sup>	+24	—
Cubebol	$C_{15}H_{26}O$	?	Oil of cubeb	M.p. 61-2	—	—	—	Phenylurethan, 186
Elemol	$C_{15}H_{26}O$	1	Oleoresin of <i>Canarium lucidum</i> A. Gray	M.p. 52 B.p. 156/17 mm.	1.5042 <sup>15</sup>	0.9400 <sup>15</sup> 0.9222 <sup>15</sup>	-10(b)	Phenylurethan, 112-3
Eudesmol	$C_{15}H_{26}O$	2	Oil from <i>Eucalyptus piperita</i> , <i>E. macarthurii</i> , and other eucalyptus oils	M.p. 83 B.p. 156/10 mm.	1.516 <sup>30</sup>	0.9884 <sup>30</sup>	+31(c)	Dihydroeudesmol, 84-5
Farnesol	$C_{15}H_{26}O$	0	Ambrette seed oil, rose oil, neroli oil	120/0.3 mm.	1.4899 <sup>30</sup>	0.894 <sup>30</sup>	—	Allophanate, 79-80
Guaiol	$C_{15}H_{26}O$	2	Oil from wood of <i>Bulnesia sarmienti</i> Lorenz	M.p. 93 B.p. 148/9 mm.	1.4716 <sup>60</sup>	0.9074 <sup>60</sup>	-30(a)	Dinitrobenzoate, 137
Lanceol	$C_{15}H_{24}O$	1	Oil from wood of <i>Santalum lanceolatum</i>	176/17 mm.	1.5074 <sup>35</sup>	0.9474 <sup>15</sup>	-77(e)	Allophanate, 114-5

(Continued)

TABLE I. Sesquiterpenoids (Continued).

Compound	Formula	No. of rings	Typical source	B.p., °C.	$n_D^{25}$	$d_4^{25}$	$[\alpha]_D^{25}$	M.p. of derivative, °C.
Alcohols <i>Continued</i>								
Ledol	$C_{15}H_{26}O$	3	Marsh tea oil from <i>Ledum palustre</i> , L.	M.p. 104-5 B.p. 290	1.4667 <sup>110</sup>	0.9814 <sup>20</sup>	+8	Chromate, 92
Macrocarpol	$C_{15}H_{26}O$	3?	Oil from leaves of <i>Cupressus macrocarpa</i>	M.p. 108	—	—	+25(a)	$\alpha$ -Naphthylurethan, 88-91
Nerolidol	$C_{15}H_{26}O$	0	Neroli oil, oil from wood of <i>Myrciyan peritvae</i> (Royle) Klotzsch	127/5 mm.	1.4802 <sup>20</sup>	0.880 <sup>15</sup>	+13	Phenylurethan, 37-8
Partheniol	$C_{15}H_{26}O$	2	Guayule resin	M.p. 127-8	—	—	+117(c)	Cinnamate, 125-6
Patchouli alcohol	$C_{15}H_{26}O$	3	Patchouli oil	M.p. 56 B.p. 140/8 mm.	1.5029 <sup>55</sup>	0.9924 <sup>65</sup>	-97(c)	—
$\alpha$ -Santalol	$C_{15}H_{26}O$	3	Indian sandalwood oil	167/14 mm.	1.5017 <sup>25</sup>	0.9770 <sup>25</sup>	+10(e)	Allophanate, 162-3
$\beta$ -Santalol	$C_{15}H_{26}O$	2	Indian sandalwood oil	178/17 mm.	1.5100 <sup>25</sup>	0.9717 <sup>25</sup>	-87(e)	Allophanate, 159-60
Sesquibenzhiol	$C_{15}H_{26}O_2$	2	Oil from <i>Chamaecyparis formosensis</i>	M.p. 120-30	—	—	-36	—
Sesquibenzhiol	$C_{15}H_{26}O$	2	Oil from <i>Chamaecyparis formosensis</i>	137/3 mm.	1.5220	0.9977 <sup>15</sup>	+9	—
Sesquicryptol	$C_{15}H_{26}O$	1?	Oil from leaves <i>Cryptomeria japonica</i> Don.	M.p. 49-51 B.p. 174/20 mm.	1.4978 <sup>50</sup>	0.9031 <sup>14</sup>	+23(c)	—
Sesquigoyol	$C_{15}H_{26}O$	2?	Oil from <i>Pinus formosana</i> Hayata	M.p. 137 B.p. 160-5/8 mm.	—	—	+93	Dihydrosesquigoyol, 121
Torreyol	$C_{15}H_{26}O$	2	Oil from leaves of <i>Torreya nucifera</i> S. et Z.	M.p. 140	—	—	+107	Dihydrotorreyol, 106-7
Aldehyde								
Nortricycloekasantalal	$C_{15}H_{16}O$	3	East Indian sandalwood oil	87/6 mm.	1.4839 <sup>20</sup>	0.9938 <sup>20</sup>	-38	Semicarbazone, 223-4
Ketones								
Acorone	$C_{15}H_{24}O_2$	2	Oil of <i>Acorus callamus</i> L.	M.p. 100-1	—	—	+139(a)	Disemicarbazone, 205-7
Isoacorone	$C_{15}H_{24}O_2$	2	Oil of <i>Acorus callamus</i> L.	M.p. 96-7	—	—	-92(a)	Semicarbazone, 196-7
$\alpha$ -Atlantone	$C_{15}H_{26}O$	1	Oil from <i>Cedrus libanotica</i> Link and other cedarwoods	123/1 mm.	1.5181 <sup>20</sup>	0.9562 <sup>20</sup>	+25	—
$\gamma$ -Atlantone (mixture)	$C_{15}H_{26}O$	1						



$\alpha$ -Cyperone	$C_{15}H_{24}O$	2	Oil from tubers of <i>Cyperus rotundus</i>	177/20 mm.	1.5283 <sup>25</sup>	0.9946 <sup>25</sup>	+138(c)	Oxime, 150
Eremophilone	$C_{15}H_{24}O$	2	Wood oil from <i>Eremophila mitchelli</i>	M.p. 41-2 B.p. 171/15 mm.	1.5182 <sup>25</sup>	0.9994 <sup>25</sup>	-207(e)	Semicarbazone, 202-3
Hydroxyeremophilone	$C_{15}H_{24}O_2$	2	Wood oil from <i>Eremophila mitchelli</i>	M.p. 66-7 B.p. 190/22 mm.	1.5564 <sup>25</sup>	1.062 <sup>25</sup>	+153(d)	Benzoate, 119-20
Ishwarone	$C_{15}H_{24}O$	?	Oil from roots of <i>Aristolochia indica</i>	120/1 mm.	1.5122 <sup>30</sup>	1.029 <sup>30</sup>	-47	Oxime, 133
Perezone	$C_{15}H_{26}O_3$	1	Roots of <i>Trixis pipilzahuac</i> Schaffner	M.p. 103-4	—	—	-17(g)	Anilino derivative, 135-6
Turnerone	$C_{15}H_{24}O$	1	Oil from rhizomes of <i>Curcuma longa</i> L.	114/10 mm.	1.5175 <sup>20</sup>	0.9502 <sup>4</sup>	+14	—
$\alpha$ -Turnerone	$C_{15}H_{24}O$	1	Oil from rhizomes of <i>Curcuma longa</i> L.	160/10 mm.	1.5219 <sup>20</sup>	0.9634 <sup>20</sup>	+82	Semicarbazone, 108-9
$\alpha$ -Vetivone	$C_{15}H_{24}O$	2	Oil from vetiver roots	M.p. 51 B.p. 153/4 mm.	1.5378 <sup>20</sup>	1.0074 <sup>20</sup>	+225(a)	Semicarbazone, 222-3
$\beta$ -Vetivone	$C_{15}H_{24}O$	2	Oil from vetiver roots	M.p. 44 B.p. 154/4 mm.	1.5309 <sup>20</sup>	1.0001 <sup>20</sup>	-24(a)	Semicarbazone, 228-9
Zierone	$C_{15}H_{24}O$	3?	Oil from <i>Zieria macrophylla</i>	149/18 mm.	1.514 <sup>20</sup>	0.9752 <sup>15</sup>	-146	Semicarbazone, 182
<u>Lactones</u>								
Alantolactone	$C_{15}H_{26}O_2$	2	Roots of <i>Inula helenium</i>	M.p. 76 B.p. 192/10 mm.	—	—	—	Methyl ester of derived acid, 83
Isoalantolactone	$C_{15}H_{26}O_2$	2	Roots of <i>Inula helenium</i>	M.p. 115	—	—	—	Amide of derived acid, 237-9
Artemisin	$C_{15}H_{18}O_4$	2	Seeds of <i>Artemisia maritima</i>	M.p. 205	—	—	-84(a)	Oxime, 233-4
Costus lactone	$C_{15}H_{26}O_2$	2	<i>Saussurea lappa</i> L.	211/13 mm.	1.5304	1.0891 <sup>21</sup>	+28	—
Santonin	$C_{15}H_{18}O_2$	2	Leaves and flower buds of various species of <i>Artemisia</i>	M.p. 171-2	—	—	-173(a)	$\beta$ -Oxime, 218
$\beta$ -Santonin	$C_{15}H_{18}O_2$	2	Leaves and flower buds of various species of <i>Artemisia</i>	M.p. 216-8	—	—	-137(c)	Oxime, 224
Pseudosantonin	$C_{15}H_{20}O_4$	2	<i>Artemisia maritima</i>	M.p. 183-4	—	—	-160(c)	Oxime, 203-4

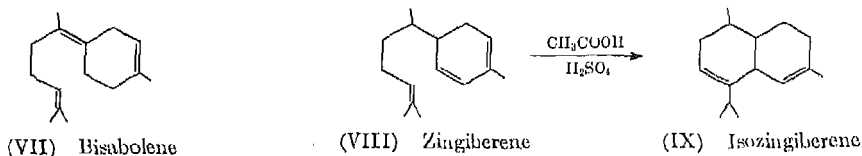
Abbreviations used with specific rotations: (a) alcohol, (b) benzene, (c) chloroform, (d) methanol, (e)  $[\alpha]_{D^{25}}$ , (f)  $[\alpha]_{D^{25}}$ , (g) ether.

with a very few exceptions find no such use since the isolation of pure components can be a very exacting process. Santonin, N.F. IX, is used as a vermifuge for ascarides (roundworm) and oxyurids (threadworm), although it is toxic. Its value as an anthelmintic is believed by some authors to have been overestimated (2,21), oil of chenopodium and ascaridole being considered superior (see Vol. 1, p. 939). Artemisin has similar physiological effects, as have some simpler molecules related to santonin.

Santonin is both manufactured in the U.S. and imported; it is sold in crystalline and powdered form in cans and drums. Cedrol is available in crude and recrystallized grades, and cedryl acetate as a 50% distilled liquid; 53,000 lb. of the acetate was produced in the U.S. in 1953, and 46,000 lb. sold at a unit value of \$2.24/lb. *Vetiverol* (vetivenol), a mixture of alcohols from vetiver oil, and its acetate are available as liquids; the acetate, often called *vetiver acetate*, was produced to the extent of 7,000 lb. in 1953; 3,000 lb. was sold at a unit value of \$29.03/lb. One thousand pounds of santolol was produced in 1953. These products, except for santonin, are used in perfumery and soaps.

### Monocyclic Hydrocarbons

**Bisabolene** (VII) (28), apart from cadinene and caryophyllene, is the most widely distributed sesquiterpenoid hydrocarbon. An isomer,  $\beta$ -bisabolene (XXVII), is obtained by reduction of lanceol (see p. 748).

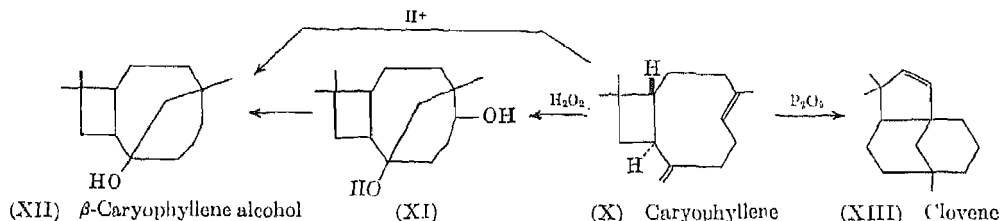


**Zingiberene** (VIII) has two of its three double bonds in conjugation (10). When zingiberene is heated with acetic and sulfuric acids at  $60^\circ\text{C}$ ., it cyclizes to give *isozingiberene* (IX), the dihydrochloride of which is formed when zingiberene is treated with hydrogen chloride. Dehydrogenation of zingiberene gives cadalene (II) in high yield.

### Bi- and Tricyclic Hydrocarbons

**Cadinene** has been assigned the structure (I) on the basis of its dehydrogenation to cadalene, of hydrogenation, and of oxidation with peroxybenzoic acid, which enabled the determination of the position of the double bonds (7).

**Caryophyllene** (X) has recently been subjected to a prolonged series of degradations which have led to the elucidation of its structure (4,9,25). Caryophyllene is remarkable for its ready cyclization under acidic conditions to give tricyclic products. One of the most important of these is  $\beta$ -caryophyllene alcohol (XII).

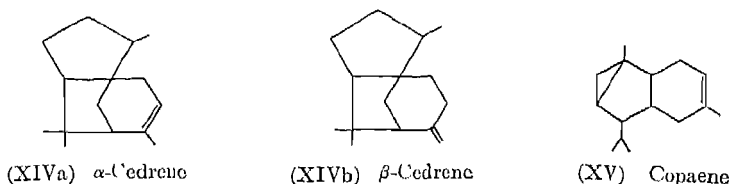


Hydrogen peroxide oxidation of the hydrocarbon yields a crystalline oxide and, as a by-product, a diol (XI), which has the same skeleton as  $\beta$ -caryophyllene alcohol, into which it has been converted. Another interesting cyclization product is the hydrocarbon *clovene* (XIII) obtained by the action of phosphorus pentoxide (22).

Caryophyllene gives a blue crystalline nitrosite, and this on treatment with alcohol regenerates a hydrocarbon, isocaryophyllene, which has recently been shown to differ from caryophyllene by the configuration about the double bond. The normal compound has the trans configuration, while the iso compound is cis.

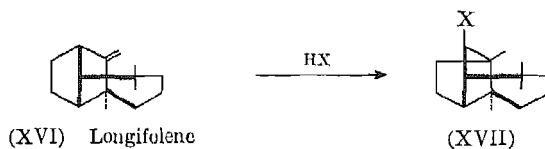
**Cedrene** occurs naturally as a mixture of products, chiefly  $\alpha$ -cedrene (XIVa) (24,33), with some  $\beta$ -cedrene (XIVb). *Cedrol* (wood camphor), the related tertiary alcohol, on dehydration affords essentially pure  $\alpha$ -cedrene.

Selenium dioxide oxidation of  $\alpha$ -cedrene in acetic anhydride solution leads to substitution of hydroxyl on the cyclohexene methyl group to give *prim-cedrenol*, as the acetate; this alcohol is also a constituent of the higher-boiling fractions of cedarwood oil.



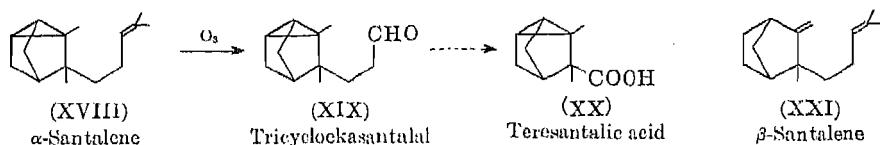
**Copaene** appears to be a rarer constituent of essential oils. On treatment with hydrogen chloride it gives cadinene dihydrochloride, and on sulfur dehydrogenation it forms cadalene (II). The formula (XV) has been proposed and supported by some degradational evidence (6).

**Longifolene** (XVI) rearranges to form a crystalline *hydrochloride* and *hydrobromide*, (XVII, X = Cl or Br), the constitutions of which were determined by x-ray analysis (20). Subsequent chemical work has been in agreement with these conclusions.



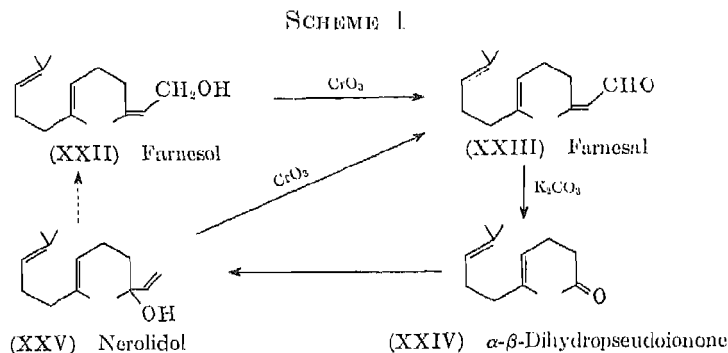
From molecular rotation considerations, longifolene has been related to the glyceraldehyde convention, and its absolute configuration is, therefore, known.

$\alpha$ - and  $\beta$ -**Santalenes** can only be separated with considerable difficulty from each other in the sandalwood oil in which they occur.  $\alpha$ -Santalene (XVIII) (29) is tricyclic, and it has been ozonized to give an aldehyde, *tricycloekasantalal* (XIX), which has been degraded to *teresantalic acid* (XX), also a constituent of the oil.  $\beta$ -Santalene is bicyclic and is probably represented by (XXI).



## Acyclic Alcohols

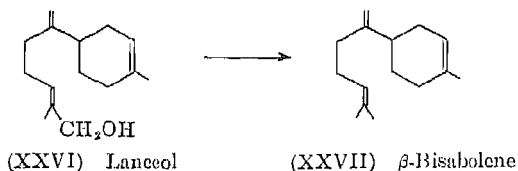
**Farnesol** (XXII) is a primary alcohol as shown by its oxidation with chromic acid to the aldehyde *farnesal* (XXIII) and, on further conversion, to the acid farnesic acid (16, 19). Also formed when farnesal is heated with potassium carbonate is  $\alpha,\beta$ -dihydropseudoionone (XXIV). See Scheme 1.



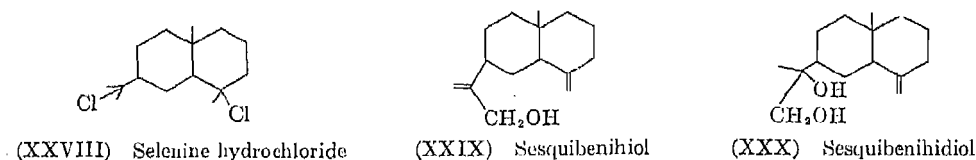
**Nerolidol** (XXV) is a tertiary alcohol isomeric with farnesol. Chromic acid oxidation gives, with rearrangement, farnesal (XXIII), and treatment with acetic anhydride leads to the production of some farnesyl acetate. Optically inactive nerolidol has been synthesized from (XXIV). See Scheme 1.

## Cyclic Alcohols

**Lanceol** (XXVI) contains three ethylenic linkages none of which is conjugated; it is also an allylic alcohol. Recently it has been converted by reduction with sodium and liquid ammonia into  $\beta$ -bisabolene (XXVII), an isomer of bisabolene (VII).

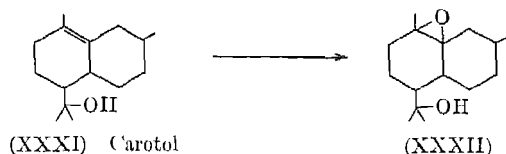


**Eudesmol** (seleninol), although obtained from eucalyptus oils in crystalline form, is a mixture of two isomers:  $\alpha$ - (1,2,3,4,4a,5,6,8a-octahydro- $\alpha,\alpha,4a,8$ -tetramethyl-2-naphthalenemethanol) and  $\beta$ -eudesmol, the corresponding decahydro-8-methylene compound (III) (27). Both isomers give eudalene (IV) on dehydrogenation. Treatment with hydrogen chloride gives a compound believed to be identical with *selenine hydrochloride* (XXVIII).

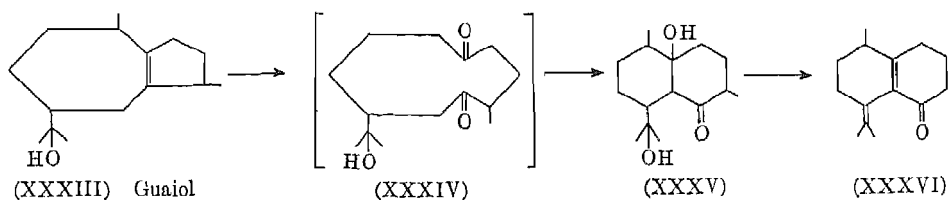


**Sesquibenihiol** (XXIX), a primary alcohol, and **sesquibenihiol** (XXX), a primary-tertiary alcohol, occur together.

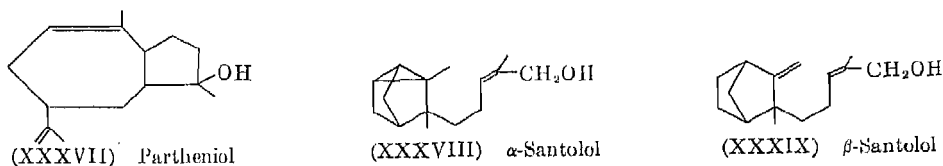
**Carotol** (XXXI) is converted by peroxyphthalic acid to an oxide (XXXII), which occurs with carotol in the same oil. The tertiary hydroxyl group of carotol is easily eliminated by formic acid to give a mixture of hydrocarbons.



**Guaiol** (XXXIII), a crystalline alcohol, gives guaiazulene (V) (23) on sulfur dehydrogenation. Raney nickel hydrogenation under forcing conditions yields dihydroguaiol. An interesting conversion to the cadalene skeleton is achieved by ozonolysis of guaiol through, presumably, the diketone (XXXIV) to the dihydroxy ketone (XXXV). This on treatment with base readily loses two molecules of water to give the dienone (XXXVI), which has been dehydrogenated with palladized charcoal to cadalene (II).



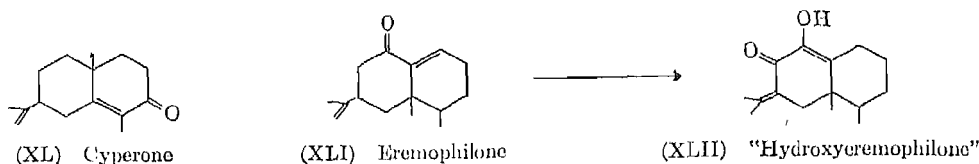
**Partheniol** (XXXVII) occurs as the cinnamate and is isolated in the refining of guayule rubber. It contains two double bonds and a tertiary alcoholic group which may be dehydrated with potassium bisulfate to give the 1-methylene derivative (*anhydripartheniol*). This in turn gives guaiazulene (V) on sulfur dehydrogenation (15).



**α- and β-Santalols** are both primary alcohols, and their separation, as for the santalenes, is extremely difficult. Ozonolysis of **α-santolol** (XXXVIII) gives tri-cycloekasantal (XIX).

### Ketones

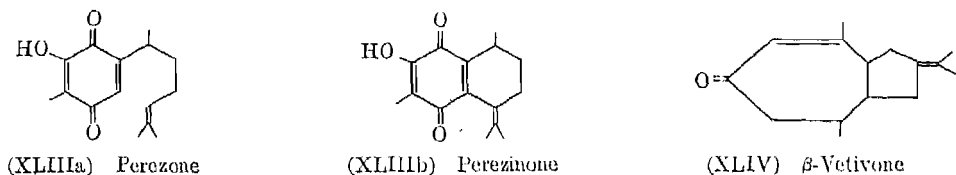
**α-Cyperone** (XI) contains two ethylenic linkages (31), one of which is in conjugation with the carbonyl group, as is shown by the ultraviolet absorption spectrum and by its reduction with sodium and alcohol to the *ar*-dihydro alcohol (dihydro-**α**-cyperol). Dehydrogenation of this gives eudalene (IV).



**Eremophilone** (XLI) contains two ethylenic linkages and can be reduced with sodium and alcohol to the *ar*-dihydro alcohol (dihydroeremophilol), which on selenium dehydrogenation gives eudalene (IV).

Eremophilone is unique among the sesquiterpenoids in that its carbon skeleton cannot be built up from three isoprene units (11,32). Evidence for the position of the angular methyl group was obtained by degradation of "*hydroxyeremophilone*" (XLII), which is obtained by treatment of eremophilone with hydrogen peroxide to give the oxide, which, on heating with acetic anhydride and sodium acetate followed by alkaline hydrolysis, is rearranged to (XLII). It also occurs with eremophilone in the essential oil.

**Perezone** (XLIIIa) is the only known example of a sesquiterpenoid quinone. It is golden yellow and is reduced to a leuco compound which is easily oxidized in air back to perezone. The hydroxyl group is acidic and forms metallic salts. Perezone can be cyclized to the quinone *perezinone* (XLIIIb) via the 5-anilino and 5-hydroxy derivatives.



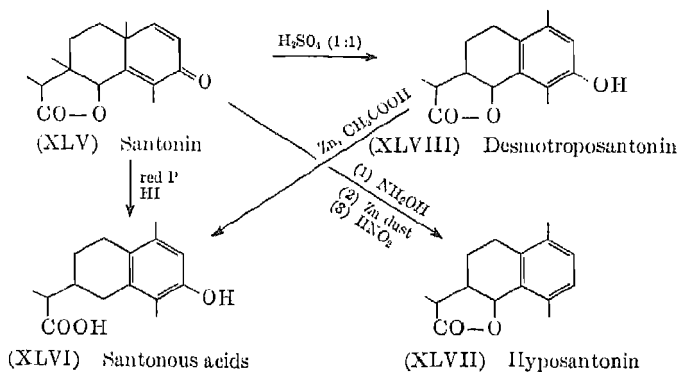
$\alpha$ - and  $\beta$ -**Vetivones** are stereoisomers. Catalytic hydrogenation of  $\beta$ -vetivone (XLIV) gives the saturated optically inactive tetrahydrovetivol, dehydrogenation of which gives vetivazulene (VI), also obtained from  $\beta$ -vetivone itself.

### Lactones

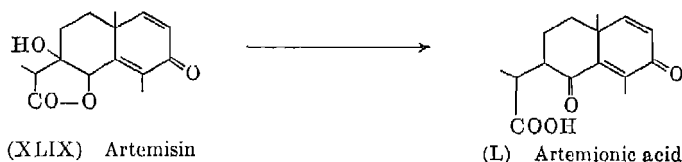
**Santonin** (XLV) is an unsaturated ketonic lactone dissolving easily in alkali and giving the usual ketonic derivatives (8). On hydrogenation it affords a mixture of saturated ketonic lactones,  $\alpha$ - and  $\beta$ -tetrahydrosantonin. As shown in Scheme 2, it can undergo aromatization of the quinonoid ring, with concomitant methyl migration, to form three types of products: (1) a mixture of phenolic acids, (+)- and ( $\pm$ )-*santonous acids* (XLVI); (2) a lactone, *hyposantonin* (XLVII), via santonin oxime and the amine; and (3) (-)-*desmotroposantonin* (XLVIII), which can be reduced to (-)-santonous acid.

The chemistry of santonin is vastly complicated by the numerous possibilities of isomers of each of the above types of compounds (18). Theoretically, sixteen active santonins should be possible, although only two, santonin and  $\beta$ -santonin, are known. Eight desmotroposantonins could exist, and of these four are known, and, corresponding to the eight desmotroposantonins, four santonous acids are possible, all of which have now been prepared.

SCHEME 2



**Artemisin** (XLIX) is an unsaturated ketonic lactone containing a tertiary hydroxyl group which can, however, be acetylated. On treatment with strongly acidic reagents, artemisin gives a naphtholic acid, artemisic acid, whereas, when treated with dilute sulfuric acid below 60°C., an isomeric lactone, desmotropoartemisin, is obtained, thus closely paralleling santonin. Acetylartemisin (or artemisin itself) on alkaline hydrolysis yields *artemionic acid* (L) (5,34).



### Bibliography

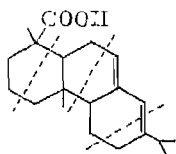
- (1) Arnold, H., *Die Chemie*, **56**, 7 (1943).
- (2) Asahina, Y., and Momose, T., *Proc. Imp. Acad. Tokyo*, **14**, 112 (1938).
- (3) Barton, D. H. R., "Sesquiterpenoids," in Rodd, *Chemistry of the Carbon Compounds*, Elsevier, Houston, Tex., and Amsterdam, 1953, Vol. IIB, ch. XIV.
- (4) Barton, D. H. R., *et al.*, *J. Chem. Soc.*, **1952**, 2210; and later papers in this series.
- (5) Bertolo, P., *Atti accad. Lincei*, **1** [6], 436 (1925); and previous parts of this series.
- (6) Briggs, L. H., and Taylor, W. I., *J. Chem. Soc.*, **1947**, 1338.
- (7) Campbell, W. F., and Soffer, M. D., *J. Am. Chem. Soc.*, **64**, 417 (1942).
- (8) Clemo, G. R., Haworth, R. D., and Walton, E., *J. Chem. Soc.*, **1929**, 2368; **1930**, 1110.
- (9) Dawson, T. L., and Ramage, G. R., *J. Chem. Soc.*, **1951**, 3382.
- (10) Eschenmoser, A., and Schinz, H., *Helv. Chim. Acta*, **33**, 171 (1950).
- (11) Geissman, T. A., *J. Am. Chem. Soc.*, **75**, 4008 (1953).
- (12) Gildemeister, E., and Hoffmann, F., *Die Aetherische Öle*, 3rd ed., Leipzig, 1928-31.
- (13) Gordon, M., *Chem. Revs.*, **50**, 127 (1952).
- (14) Guenther, E., *The Essential Oils*, Van Nostrand, N.Y. 1947-52, Vols. I-VI.
- (15) Haagen-Smit, A. J., and Fong, C. T. O., *J. Am. Chem. Soc.*, **70**, 2075 (1948).
- (16) Harries, C., and Haarmann, R., *Ber.*, **46**, 1737 (1913).
- (17) Haworth, R. D., *Ann. Repts. on Progr. Chem. (Chem. Soc. London)*, **34**, 393 (1937).
- (18) Huang-Minlon, *J. Am. Chem. Soc.*, **70**, 611 (1948).
- (19) Kerschbaum, M., *Ber.*, **46**, 1732 (1913).
- (20) Moffet, R. H., and Rogers, D., *Chemistry & Industry*, **1953**, 916.
- (21) Oelkers, H. A., and Rathje, W., *Trop. Diseases Bull.*, **39**, 767 (1942).
- (22) Nickon, A., *Perfumery Essent. Oil Record*, **45**, 149 (1954).
- (23) Pfau, A. S., and Plattner, P. A., *Helv. Chim. Acta*, **19**, 858 (1936).

- (24) Plattner, P. A., *et al.*, *Helv. Chim. Acta*, **36**, 1845 (1953).  
 (25) Robertson, J. M., and Todd, G., *Chemistry & Industry*, **1953**, 437.  
 (26) Ruzicka, L., *Über Konstitution und Zusammenhänge in der Sesquiterpenreihe*, Berlin, 1928.  
 (27) Ruzicka, L., *et al.*, *Helv. Chim. Acta*, **14**, 1132 (1931).  
 (28) Ruzicka, L., *et al.*, *Helv. Chim. Acta*, **15**, 3 (1932); *Ann.*, **468**, 133, 143 (1929).  
 (29) Semmler, F. W., *et al.*, *Ber.*, **49**, 2563 (1916); and previous papers in this series.  
 (30) Simonsen, J. L., and Barton, D. H. R., *The Terpenes*, Cambridge Univ. Press, 1952, Vol. III.  
 (31) Simonsen, J. L., *et al.*, *J. Chem. Soc.*, **1936**, 667; **1937**, 760.  
 (32) Simonsen, J. L., *et al.*, *J. Chem. Soc.*, **1932**, 2744; **1938**, 764, 774; **1940**, 415; **1941**, 60.  
 (33) Stork, G., and Breslow, R., *J. Am. Chem. Soc.*, **75**, 3291 (1953).  
 (34) Tettweiler, K., *et al.*, *Ann.*, **492**, 105 (1932).

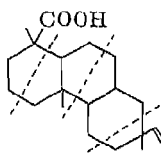
P. DE MAYO

## DITERPENOIDS

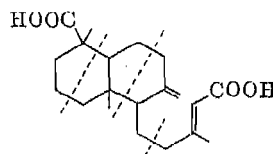
The diterpenoids are composed of four 2-methylbutane units, arranged in accordance with the isoprene rule, with additional functionality such as ethylenic unsaturation and carboxyl, phenol, and alcohol groups. Adherence to the isoprene rule is illustrated by the formulas for abietic acid (I), dextropimaric acid (II), agathic acid (III), ferruginol (IV), and camphorene (V). While most of the diterpenoids are cyclic (tricyclic or bicyclic capable of cyclization to tricyclic), phytol and a few others are acyclic.



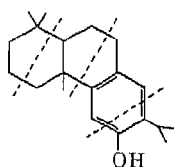
(I) Abietic acid



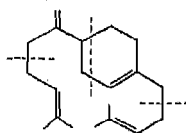
(II) Dextropimaric acid



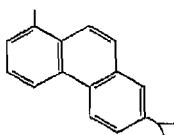
(III) Agathic acid



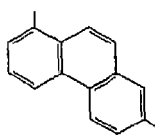
(IV) Ferruginol



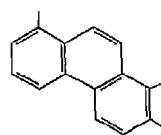
(V) Camphorene



(VI) Retene



(VII) Pimanthrene



(VIII) 1,7,8-Trimethylphenanthrene

The extensive literature on the structure elucidations of most of these compounds has been reviewed and described by Fieser (10) and Barton (1). The importance of the technique of dehydrogenation to obtain aromatic hydrocarbons in structure proofs is manifested throughout. The method was first applied by Vesterberg (35), who obtained retene (VI) from the dehydrogenation of abietic acid with sulfur. In general,



on dehydrogenation the abietic-type acids (see Vol. 11, p. 787) yield retene and the pimanic-type yield pimanthrene (VII). Ruzicka (30) obtained 1,7,8-trimethylphenanthrene (VIII) from the dehydrogenation of a cyclized derivative of agathic acid (III). Accordingly, three main classes of diterpenoids exist and are distinguishable, for the most part, by the substances obtained on dehydrogenation.

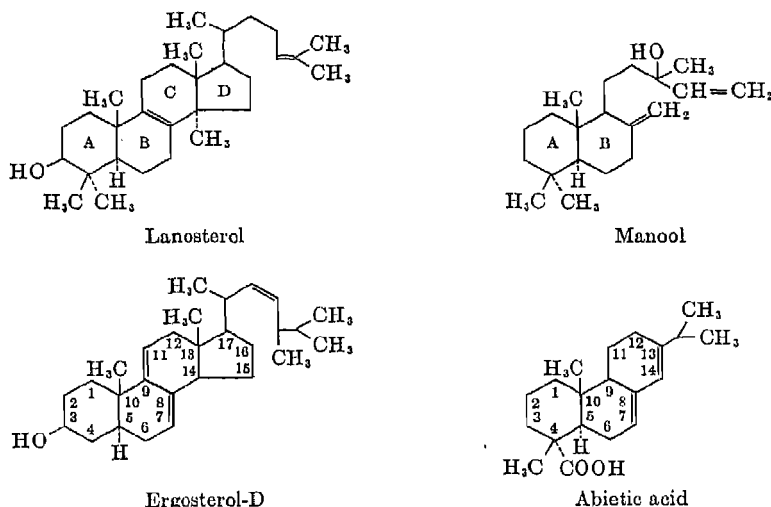


Figure 1.

The resin acids, as typified by abietic acid, and some other diterpenoids such as manool have been related to the steroids stereochemically in the manner shown in Fig. 1. The structural formulas for abietic acid and manool are written in the inverted form, and the steroid numbering system and stereochemical conventions are used for purposes of comparing the structural similarities. (The methyl groups and the  $\alpha$ -hydrogen atoms, attached by dotted lines, are shown in Fig. 1, contrary to

TABLE I. Diterpenoids of Unknown Structure.

Name	Formula	M.p., °C.	$[\alpha]_D$	Source	Reference
Hinokiol	$C_{20}H_{30}O_2$	234	+74°	<i>Chamaecyparis obtusa</i> , Siebet Zucc.	(19)
Totarol	$C_{20}H_{30}O$	132	+41°	Totara tree	(34)
Marrubiin	$C_{20}H_{34}O_4$	160	+46°	Horchound, <i>Marrubium vulgare</i> L.	(24)
Cryptopimaric acid	$C_{20}H_{30}O_2$	161	-19°	<i>Cryptomeria japonica</i>	(18)
Rubiabietic acid	$C_{20}H_{30}O_2$	162	(-)	<i>Ceroplastes rubens</i> M.	(23)
Rubenic acid	$C_{20}H_{30}O_3$	88	(i)	<i>Ceroplastes rubens</i> M.	(23)
Rubenol	$C_{20}H_{32}O_2$	liq.	(i)	<i>Ceroplastes rubens</i> M.	(23)
Rimnene	$C_{20}H_{32}$	55	+45°	<i>Daceyidium cupressinus</i>	(25)
Phyllocladene	$C_{20}H_{32}$	98	+16°	Essential oils	(4)
Isophyllocladene	$C_{20}H_{32}$	112	+24°	—	(5)
Mirene	$C_{20}H_{32}$	59	+44°	<i>Podocarpus ferrugineus</i>	(6)
Kaurene	$C_{20}H_{30}$	60	-1°	<i>Agathis australis</i>	(16)
Cupressene	$C_{20}H_{32}$	75	+59°	<i>Cupressus macrocarpa</i>	(5)
Podocarpenes	$C_{20}H_{32}$				
$\alpha$ -		51	-112°	<i>P. macrophylla</i>	(6,26)
$\beta$ -		liq.	-16°	<i>Scialopitys verticillata</i>	
$\gamma$ -		65	-27°	—	

the usual practice for terpenes.) The A and B rings in the diterpenoids have been shown to be *trans* (or *allo*) by a consideration of the thermodynamic dissociation constants of a  $C_{11}$ -tricarboxylic acid obtained in the vigorous oxidative degradation of abietic acid. See *Sterols and steroids*; see also *Stereochemistry (organic)*, Vol. 12, p. 858.

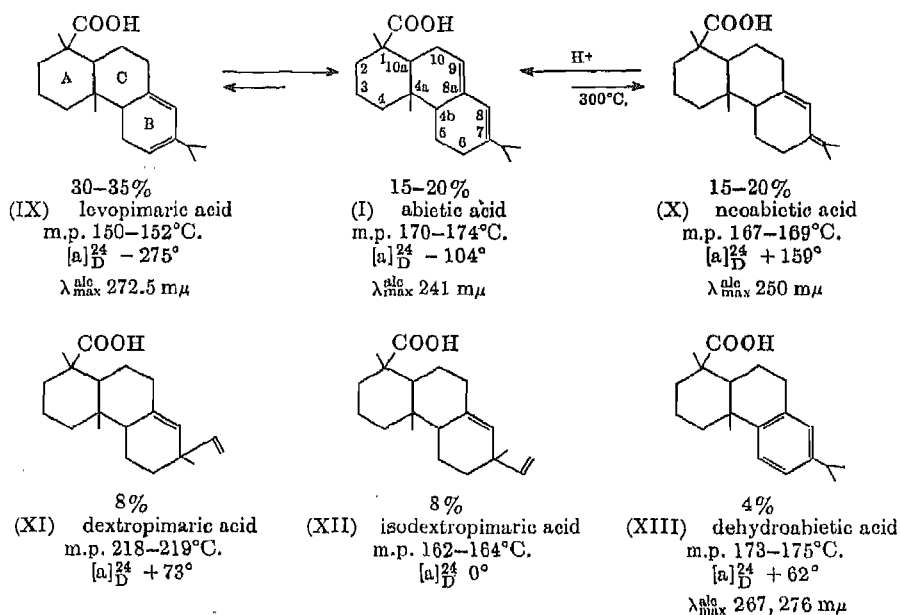
Of the diterpenes, the acids are the most abundant and familiar; of the diterpene acids, the resin acids from pine oleoresins have been exploited commercially and are the best known. Therefore, these acids will be described first, and then in turn other acids, phenols, alcohols, and hydrocarbons. Some diterpenoids of unknown structure are listed in Table I.

### Acids

#### RESIN ACIDS FROM PINE OLEORESINS

The acids, all tricyclic, occurring as primary constituents in oleoresins of *Pinus palustris* (longleaf pine) and *P. caribaea* (slash pine) are shown in Scheme 1, with the average percentages found and some of their properties ( $[\alpha]_D^{25}$  was determined on 1% solutions in absolute alcohol).

SCHEME 1



**Abietic acid** (I),  $C_{20}H_{30}O_2$ , contains two double bonds distributed between two rings, as shown by an ultraviolet absorption spectrum with chief absorption band at  $241 \text{ m}\mu$ . A good yield of retene is obtained upon the dehydrogenation of abietic acid with sulfur, selenium, or noble-metal catalysts on carbon supports.

Abietic acid has been found as a component of the fresh oleoresin (13) of *P. palustris* and hence is a primary resin acid. It is the major component (50–55%) of commercial rosins (*q.v.*), having been formed by the transformation of other two-double-bond resin acids during manufacture. It is sensitive not only to acids and heat but also to air and light and must therefore be stored in evacuated tubes away from light.

Although it is an end product of heat treatment and acid isomerization of other resin acids, it is partially isomerized to neoabietic acid on moderate heat treatment and under the influence of a catalyst disproportionates to produce mixtures of dehydro-, dihydro-, and tetrahydroabietic acids. With its trans configuration of double bonds conjugated between two rings, abietic acid does not react with maleic anhydride under nonisomerizing conditions.

Abietic acid can be isolated from a mixture of acids such as exists in wood or gum rosins by a two-step process: (1) isomerization of rosin with mineral acid in alcohol solution or boiling acetic acid to transform the resin acid isomers to abietic acid; (2) selective precipitation of the abietic acid from solutions of the isomerized rosin in acetone with diamylamine. The diamylamine salt of abietic acid is purified by fractional recrystallization, and the acid is obtained pure to the extent of 40% of the rosin with constants noted in Scheme 1.

**Levopimaric acid (IX)**,  $C_{20}H_{30}O_2$ , an abietic-type acid in spite of its name, is the major component of the oleoresins of *P. palustris* and *P. caribaea* and other pine and fir trees. The two double bonds have been shown to be conjugated within ring B (cis configuration) by the ultraviolet absorption spectrum of the compound demonstrating its most intense band at 272  $m\mu$  and by its ready and quantitative addition of maleic anhydride at room temperature without the influence of strong acid. The maleic anhydride adduct has a m.p. 226–227°C. and is used as a means of characterizing the acid.

Levopimaric acid is highly susceptible to strong mineral acid. Under the influence of acid or heat, an equilibrium is established with abietic acid as the major component and levopimaric acid only in trace quantities. Levopimaric acid is much less light- and air-sensitive than abietic acid and can be stored under normal conditions. Early methods of isolating levopimaric acid consisted of crystallization of a fraction of the oleoresin from alcohol, preparation and fractionation of the sodium salts, and regeneration of the acid. This and other methods resulted in low yields so that only small amounts of material were available for the excellent work by Ruzicka and co-workers in the elucidation of the structure of levopimaric acid.

The acid can be obtained only from the oleoresin since it is transformed in the working of the oleoresins to obtain the two fractions turpentine (*q.v.*) and gum rosins. An efficient method (14) for its isolation consists of the isolation of the total acids of the oleoresin by means of cyclohexylamine salts and precipitation and fractionation of the butanolamine salt of levopimaric acid from this mixture.

**Neoabietic acid (X)**,  $C_{20}H_{30}O_2$ , is the dextrorotatory component of the oleoresins of pines frequently referred to in the extensive literature on the isolation of pure components of the acid fractions of oleoresinous exudates. It was often isolated as one of several components of a mixture of resin acids with optical rotations varying from +11° to +44°, thought to be a pure compound because of the lack of a method for their separation. It was isolated (14) in pure form,  $[\alpha]_D^{24} +159^\circ$ , after the development of the amine salt method for the fractional crystallization of amine salts of resin acids and isolation of pure components.

In neoabietic acid, also an abietic-type acid, the two double bonds are conjugated, one exocyclic (in an isopropylidene group) with respect to the other as shown by an intense band at 250  $m\mu$  in the ultraviolet region and by the isolation of acetone and an  $\alpha,\beta$ -unsaturated ketone on ozonolysis.

Like levopimaric acid, neoabietic acid is isomerized by acid or heat to an equilib-

rium mixture whose major component is abietic acid. At 300°C. in an inert atmosphere, however, abietic acid forms neoabietic acid. The latter is less sensitive than abietic acid to degradation by light and atmospheric oxygen so that it can be stored without added precautions.

**Dextropimaric acid (XI)**,  $C_{20}H_{30}O_2$ , is one of the earliest known resin acids, having been isolated by Cailliot in 1874. It is a pimaric-type acid (see Vol. 11, p. 779) and is distinguished from the abietic-type acids by the following: (1) on dehydrogenation it yields pimanthrene; (2) the two double bonds are not conjugated and cannot be brought into conjugation because of the gem configuration of the vinyl and methyl groupings at carbon 7; and (3) it is stable to heat and strong acid and is not oxidized by atmospheric oxygen.

Dextropimaric acid can be identified readily by catalytic hydrogenation to its sparingly soluble dihydro derivative, m.p. 240°C., formed by saturation of the vinyl group. It is one of the minor components of oleoresins as well as commercial rosins. A procedure for its isolation by crystallization of its sparingly soluble sodium salt was improved upon by Palkin and Harris (27). A simpler and more efficient method of isolation described recently (15) is based on the observation that both pimaric-type acids (dextro- and isodextropimaric acids) are more volatile than the other acids in wood and gum rosins. Rosin is distilled with high reflux ratio at 136–200°/1 mm. to obtain a 12% distillate. The acid components of the distillate are essentially the two acids and are separated from the neutral components by extraction with dilute alkali, whereupon the mixture is separated into the two pure components by fractional crystallization of the butanolamine salts.

**Isodextropimaric acid (XII)** is the C(7)-epimer of dextropimaric acid. It escaped the notice of the earlier workers because its sodium salt is more soluble than that of dextropimaric acid; it was isolated by Harris (15) by making use of its butanolamine salt being more insoluble than that of the epimer. The butanolamine salt of isodextropimaric acid can be precipitated from a methyl acetate solution of a mixture of acids from which the abietic-type acids have been removed by means of the maleic anhydride adduct. Its stability to heat and acid isomerization and to attack by atmospheric oxygen is essentially the same as that of dextropimaric acid.

**Dehydroabietic acid (XIII)** was regarded only as a transformation product of abietic-type acids until it was detected in the oleoresins of *P. palustris* and *P. caribaea*. Accordingly, it must be considered a primary resin acid. It was first prepared pure by Fieser and Campbell (8) by the selenium dioxide oxidation of abietic acid followed by dehydration of the 6-hydroxy compound. Low absorption in the ultraviolet region at 267 m $\mu$  and 276 m $\mu$  indicates a hydroaromatic nucleus. A convenient process (9) for its preparation consists of the sulfonation of a disproportionated mixture of abietic-type acids, separation of the crystalline sulfonic acid from water-insoluble material, and desulfonation by acid hydrolysis at 135°C. The extensive work with dehydroabietic acid currently under way in several laboratories might indicate it as a future important intermediate in the preparation of compounds with physiological activity related to the steroids.

#### OTHER ACIDS

**Agathic acid** (agathenedicarboxylic acid) (III) (see also Vol. 11, p. 677),  $C_{20}H_{28}O_4$ , is a bicyclic acid, m.p. 203–204°C.,  $[\alpha]_D^{25} +52$  to  $+56^\circ$  (alcohol). It was isolated by

Ruzicka in 1929. The structure now accepted was determined entirely by Ruzicka and his co-workers (29).

It is generally assumed that fossil resins are produced when oleoresin-producing trees, the source of the resin acids described above, decay under anaerobic conditions. Agathic acid is the diterpenoid acid isolated from copal and kauri copal of a number of tropical trees obtained for the most part as fossilized material. Retene (VI) and fichtelite (XVII) have also been isolated from most rosins of the decayed pines investigated.

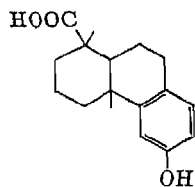
**Podocarpic acid** (XIV),  $C_{17}H_{22}O_3$ , m.p.  $193^\circ C.$ ,  $[\alpha]_{5461} +165^\circ$  (alcohol), is not, in the strict sense of the word, a diterpenoid resin acid, but its chemistry is so closely related that it is always included with diterpenes. It is the chief acidic component of the Javanese *Podocarpus cupressinus* and of the New Zealand kahikatea and rimu resins. It was first isolated by Oudemans in 1873 and much later by Sherwood and Short (32), who proved that the products of dehydrogenation with selenium are 1-methylphenanthrene and 6-hydroxy-1-methylphenanthrene. Podocarpic acid differs from 6-hydroxydehydroabietic acid both in the absence of an isopropyl group on carbon 7 and in the orientation of the methyl and carboxyl groups at carbon 1. The latter observations were proved by the work of Campbell and Todd (7).

Podocarpic acid may be characterized by its acetate, m.p.  $173-176^\circ C.$ , methyl ester, m.p.  $208^\circ C.$ , and methyl ether, m.p.  $158^\circ C.$

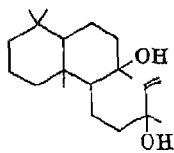
**Cativic acid**,  $C_{20}H_{34}O_2$ , is a noncrystalline acid, b.p.  $194-195^\circ C./1\text{ mm.}$ , isolated from the oleoresin of the cativa tree, where it exists as the free acid and as the ester of the primary alcohol, cativyl alcohol, derived from it. Not much is known about it other than that most probably it is diterpenoid (22) and differs from the acids already mentioned in that its carboxyl group is readily esterified.

**Vouacapenic acid**,  $C_{20}H_{28}O_3$ , m.p.  $226-229^\circ C.$ , is one of the crystalline diterpenoid acids about which little is known. Its source is the heartwood of *Vouacapoua americana* Aubl., where it exists as the methyl ester. The acid has two double bonds, and the third oxygen is probably present in an oxide linkage (34).

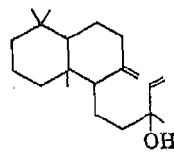
**Miropinic acid**,  $C_{20}H_{30}O_2$ , m.p.  $160^\circ C.$ ,  $[\alpha]_D -4^\circ$  (alcohol-chloroform), was isolated by Brandt (2) from the resin obtained from the miro tree, *Podocarpus ferrugineus*. It is a tricyclic diterpenoid acid with two ethylenic double bonds and yields pimanthrene on dehydrogenation. It isomerizes under the influence of mineral acid to isomiropinic acid, m.p.  $284^\circ C.$ ,  $[\alpha]_D +21^\circ$  (dioxane).



(XIV) Podocarpic acid



(XV) Sclareol

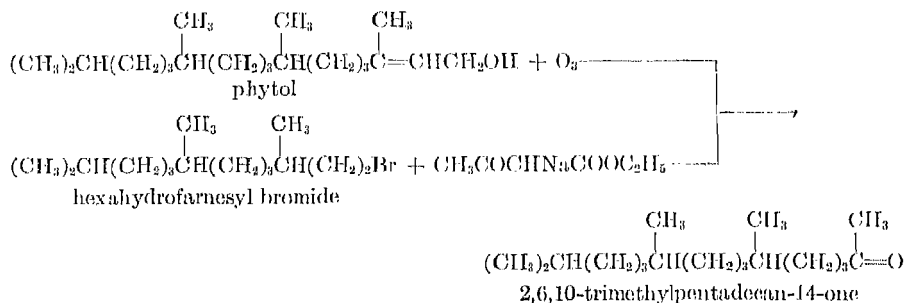


(XVI) Manool

### Alcohols and Phenols

**Phytol**,  $C_{20}H_{40}O$ , is an aliphatic diterpenoid alcohol that obeys the isoprene rule. Like isodextropimaric acid, it has a very low optical rotation,  $[\alpha]_D +0.2^\circ$ , a property that was incorrectly interpreted to signify that the compound is a racemate. It was discovered by Willstätter as the alcohol portion of the chlorophyll (*q.v.*) molecule.

It is also a part of the vitamin E and K molecules (see *Vitamins*). Its structure was proved (11) by ozonolysis to glycolaldehyde and a methyl ketone,  $C_{18}H_{36}O$ , and by the identification of the latter as 2,6,10-trimethylpentadecan-14-one by synthesis from hexahydrofarnesyl bromide and monosodium ethyl acetoacetate.



**Sclareol** (XV),  $C_{20}H_{36}O_2$ , m.p. 105–106°C., is a diterpenoid alcohol isolated from the leaves of *Salvia sclarea* L. It was shown by the following reactions to have the structure given (20,28). Hydrogenation gave the dihydro compound, m.p. 114–115°C., which on dehydration cyclized to produce a hydrocarbon which is readily dehydrogenated to 1,2,8-trimethylphenanthrene. The isolation of the latter hydrocarbon suggested a formula similar to agathic acid. Further similarity to agathic acid was shown by direct dehydrogenation of sclareol to the same trialkylated naphthalene. It is also related to manool.

**Manool** (XVI),  $C_{20}H_{34}O$ , a diterpenoid alcohol, was isolated from the wood oil of the yellow pine. It is related to sclareol and the diterpene oxides (17) since treatment with hydrogen chloride yields the same trichloro compound, m.p. 118–120°C. The position of the hydroxyl group in manool and the two double bonds were shown by two series of reactions involving direct and indirect ozonolysis (1,10). Confirmatory evidence for the structure of manool was obtained by Jeger (21) by the formation of dehydroabietane, also synthesized from abietic acid.

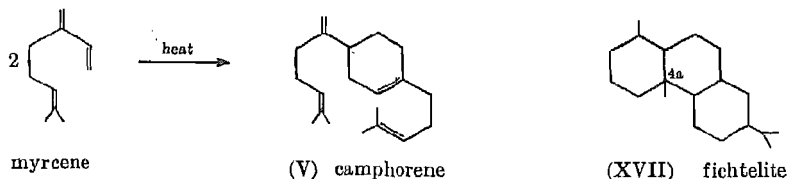
**Ferruginol** (IV),  $C_{20}H_{30}O$ , and **sugiol** (9-oxoferruginol),  $C_{20}H_{28}O_2$ , are phenolic diterpenoids. Ferruginol, b.p. 175°C./0.3 mm., was isolated as the major component of the resin of the miro tree, and sugiol, m.p. 283–284°C., was isolated from the resin of *Cryptomeria japonica* D. Don. The structure of ferruginol was elucidated by Campbell and Todd (7). Dehydrogenation with selenium gave 6-hydroxyretene. The partial synthesis of ferruginol from dehydroabietic and podocarpic acids showed the proposed structure to be correct.

Sugiol methyl ether was dehydrogenated to 6-methoxyretene after reduction of the ketone group according to the Clemmensen reaction. Further evidence was obtained by Brandt and Thomas (3) when they isolated 9-oxoferruginol from the wood of the rimu tree and showed it to be identical with sugiol. The methyl ether and acetate of ferruginol were converted to the corresponding sugiol derivatives by chromic acid oxidation.

### Hydrocarbons

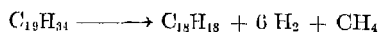
**Camphorene** (V),  $C_{20}H_{30}$ , b.p. 177°C./6 mm., was isolated from the higher-boiling hydrocarbon fraction of camphor oil. It was eventually recognized as identical with one of the constituents of the dimyrcene prepared by Harries (12) by the action of heat

on myrcene (see p. 709). Further evidence of the indicated structure is hydrogenation to the octahydro derivative, indicating the four double bonds, and oxidation of the latter with manganese dioxide to obtain terephthalic acid.



**Fichtelite** (XVII),  $C_{19}H_{34}$ , m.p.  $46^\circ\text{C}$ ., although in the strict sense of the word not a diterpenoid, is very closely related to abietic acid. It has been found repeatedly with retene in peat and lignite beds from pine forests and undoubtedly is formed from the resin acids originally present in the living pine trees.

Dehydrogenation of fichtelite with sulfur gives a good yield of retene, and on the basis of early work it was assumed to be the perhydro derivative of retene. However, the careful work of Ruzicka and Waldman (31) in the analysis of the off-gases during the dehydrogenation indicated the presence of methane in the ratio required by the equation:



This result showed conclusively the presence of an additional methyl group in a tertiary position, the 4a position being the most likely since fichtelite probably arises from the abietic-type acids in the course of the decay process.

### Bibliography

- (1) Barton, D. H. R., "The Diterpenoids" in E. H. Rodd, *Chemistry of Carbon Compounds*, Vol. IIB, Elsevier, Houston, Tex., and Amsterdam, 1953, pp. 696-725.
- (2) Brandt, C. W., and Neubauer, L. G., *J. Chem. Soc.*, **1940**, 683.
- (3) Brandt, C. W., and Thomas, B. R., *J. Chem. Soc.*, **1952**, 2442.
- (4) Briggs, L. H., *J. Chem. Soc.*, **1937**, 79.
- (5) Briggs, L. H., and Sutherland, M. D., *J. Org. Chem.*, **7**, 397 (1942).
- (6) Briggs, L. H., *et al.*, *J. Chem. Soc.*, **1950**, 955.
- (7) Campbell, W. P., and Todd, D., *J. Am. Chem. Soc.*, **64**, 928 (1942).
- (8) Fieser, L. F., and Campbell, W. P., *J. Am. Chem. Soc.*, **60**, 159 (1938).
- (9) Fieser, L. F., and Campbell, W. P., *J. Am. Chem. Soc.*, **60**, 2631 (1938); **61**, 2528 (1939).
- (10) Fieser, L. F., and Fieser, M., *Natural Products Related to Phenanthrene*, Reinhold, N.Y., 1949, pp. 40-83.
- (11) Fischer, F. G., *Ann.*, **464**, 69 (1928); Fischer, F. G. and Löwenberg, K., **475**, 183 (1929).
- (12) Harries, C., *Ber.*, **35**, 3264 (1902).
- (13) Harris, G. C., *J. Am. Chem. Soc.*, **70**, 3671 (1948).
- (14) Harris, G. C., and Sanderson, T. F., *J. Am. Chem. Soc.*, **70**, 334 (1948).
- (15) Harris, G. C., and Sanderson, T. F., *J. Am. Chem. Soc.*, **70**, 2079 (1948).
- (16) Hosking, J. R., *Rec. trav. chim.*, **49**, 1036 (1930).
- (17) Hosking, J. R., and Brandt, C. W., *Ber.*, **68**, 37 (1935); **69**, 780 (1936).
- (18) Ishiguro, T., *et al.*, *J. Pharm. Soc. Japan*, **47**, 363 (1928).
- (19) Ishiguro, T., *et al.*, *J. Pharm. Soc. Japan*, **53**, 11 (1933); **55**, 45 (1935); **59**, 116 (1939).
- (20) Janot, M. M., *Compt. rend.*, **191**, 847 (1930); **192**, 845 (1931); *Ann. chim. (Paris)*, **17**, 5 (1932).
- (21) Jeger, O., *et al.*, *Helv. Chim. Acta*, **30**, 1853 (1947).
- (22) Kalman, N. L., *J. Am. Chem. Soc.*, **60**, 1423 (1938).
- (23) Kono, M., and Maruyama, R., *J. Agr. Chem. Soc. Japan*, **13**, 177 (1937); **14**, 318 (1938); *C. A.*, **31**, 5805; **32**, 6253.

- (24) Lawson, A., and Eustice, E. D., *J. Chem. Soc.*, **1939**, 587.
- (25) McDowall, F. H., and Findlay, H. J., *J. Soc. Chem. Ind.*, **44**, 421 (1925).
- (26) Nishida, K., and Uoda, H., *J. Agr. Chem. Soc. Japan*, **7**, 157 (1931).
- (27) Palkin, S., and Harris, T. H., *J. Am. Chem. Soc.*, **55**, 3677 (1933).
- (28) Ruzicka, L., *et al.*, *Helv. Chim. Acta*, **14**, 645 (1931); **25**, 621 (1942).
- (29) Ruzicka, L., *et al.*, *Helv. Chim. Acta*, **9**, 962 (1926); **14**, 203 (1931); **26**, 2136 (1943).
- (30) Ruzicka, L., and Hosking, J. R., *Helv. Chim. Acta*, **14**, 203 (1931).
- (31) Ruzicka, L., and Waldman, W., *Helv. Chim. Acta*, **18**, 611 (1935).
- (32) Sherwood, I. R., and Short, W. F., *J. Chem. Soc.*, **1938**, 1006.
- (33) Short, W. F., *et al.*, *J. Chem. Soc.*, **1937**, 516; **1950**, 991; **1951**, 2979.
- (33a) Simonsen, J. L., and Barton, D. H. R., *The Terpenes*, 2nd ed., University Press, Cambridge, England, 1952, Vol III, Pt II.
- (34) Spoelstra, D. B., *Rec. trav. chim.*, **49**, 226 (1930).
- (35) Vesterberg, A., *Ber.*, **36**, 4200 (1903).

G. C. HARRIS

## TRITERPENOIDS

Triterpenoids by definition have skeletons consisting of thirty carbon atoms assumed to be divisible into six isoprene units. They are widely distributed in nature, occurring mainly in the plant kingdom as esters, as glycosides (saponins, *q.v.*), or in the free state. The saponins deserve special mention.

### Triterpenoid Saponins

Of the large number of triterpenoids that occur as saponins few have been obtained pure or crystalline or have been adequately characterized. Some of the better characterized members are listed in Table I.

The sugar moieties of these compounds include pentoses (arabinose, xylose, rhamnose) and hexoses (glucose, fructose, galactose) together with units of glucuronic and galacturonic acids. These saponins are soluble in water or alcohol and have the general property of lowering surface tension. It is upon this property that their commercial use largely depends. They also form stable complexes with  $3\beta$ -hydroxy steroids such as cholesterol. This property can be used for the isolation of the steroid or of the glycoside.

The general uses of saponins are a consequence of their foaming properties and lack of ingestive toxicity (see *Saponins and sapogenins*, Vol. **12**, p. 97). They are not, in general, pure preparations. Some saponins have in addition a certain medical interest; senega and quillaja have, for instance, application as expectorants (*q.v.*). Considerable interest has been aroused by the possible use of asiaticoside in the treatment of leprosy (16). Remarkable results were reported in 1945 with the crystalline glycoside, although an extract of *Centella asiatica* had been used for some time previously. It was assumed that the glycoside dissolved the waxy covering of *Bacillus leprae*, rendering it fragile and so open to attack. The sapogenin is stated to be inactive. There have been reports that asiaticoside is also of possible use in the therapy of tuberculosis. Another medicinally interesting glycoside is glycyrrhizic acid for its possible use in the treatment of Addison's disease (9).



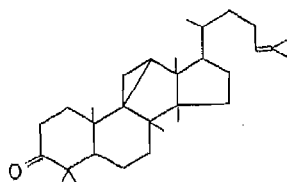
TABLE I. Triterpenoid Saponins.

Saponin	Source	M.p., °C.	$[\alpha]_D^{25}$	Sapogenin	Sugars (and derivatives)
Asiaticoside	<i>Centella asiatica</i>	232	-15.7	Asiatic acid	Glucose, rhamnose
Cyclamin	<i>Cyclamen europaeum</i>	253	—	Cyclamiretin	Glucose, arabinose
Elateoric acid	<i>Primula elatior</i>	220	-3	Elatigenin	A uronic acid, a disaccharide?
Escin (aescin)	Horse chestnut seeds	200-10	—	Escigenin (aescigenin)	Glucose, glucuronic acid, a methyl-pentose, galactose
Gypsophila saponin	Soaproot	—	—	Gypsogenin	Arabinose, rhamnose, glucose, galactose
Glycyrrhizic acid	Liquorice plant	220	+58.6	Glycyrrhetic acid	A hexuronic acid
$\alpha$ -Hederin	Ivy leaves	256	+9.7	Hederagenin	Fructose, arabinose, rhamnose
Quillaja (quillaia) saponin	Quillaja bark	—	—	Quillaic acid	Galactose
Quinovin	Cinchona bark	235	+59	Quinovic acid	D-Quinovose (isorhodeose)
Saponin	<i>Bassia longifolia</i>	235-40	—	Bassic acid	Rhamnose, arabinose, glucose
Soapnut saponin	<i>Sapindus</i> spp.	—	—	Hederagenin	Fructose, arabinose, rhamnose
Sugar-beet saponin	Sugar beets	215	+31	Oleanolic acid	Glucuronic acid

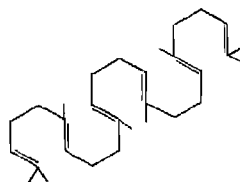
<sup>a</sup> Rotations are in alcohol.

### Classification of Triterpenoids

The triterpenoids can be classified most easily on the basis of the number of rings present, chiefly 4 or 5. The relationship of various complex compounds to simpler, parent, compounds—usually monohydric alcohols—then allows of the classification of smaller groups. However, with the recent elucidation of the structures of the **tetracyclic triterpenoids**, which have been found to be nonisoprenoid (for example, lanosterol, agnosterol) and the still more recent determination of the structures of eburicoic acid and the polyporenic acids (which have 31 carbon atoms and an ergostane-type side chain), the closeness of the relationship of these trimethylated steroids to the steroids proper has become clearer, and they have accordingly been classed with the steroids (see *Sterols and steroids*). The conversion of cholesterol into the naturally occurring tetracyclic triterpenoid dihydrolanosterol has now been accomplished and so constitutes the first total synthesis of a tetracyclic triterpenoid. It confirms, also, the close stereochemical relationship between this group and the steroids (21).



(I) Cycloartenone



(II) Squalene

Recently the structure of *cycloartenone* has been established as (I), which thus places it with the tetracyclic group, although in fact, it is pentacyclic.

There remain, therefore, for consideration here only the pentacyclic triterpenoids as a large class and the classes consisting of the important single members squalene (acyclic) and ambrein (tricyclic). A list of the more important triterpenoids is given in Table II.

TABLE II. Triterpenoid Sapogenins.

Sapogenin	Formula	Source	M.p., °C.	$[\alpha]_D^{25}$	M.p. of derivative, °C.
<u>Acyclic</u>					
Squalene	$C_{30}H_{50}$	<i>Centrophorus granulatus</i>	B.p. 242 <sub>4</sub>	$d_4^{25} 0.8592$ $n_D^{25} 1.4990$	
<u>Tricyclic</u>					
Ambrein	$C_{30}H_{52}O$	Ambergris	83	+21 <sup>b</sup>	
<u>Pentacyclic</u>					
<i>β-Amyrin Group</i>					
β-Amyrin	$C_{30}H_{50}O$	Manila elemi resin	197	+89	Acetate, 241
α-Boswellic acid	$C_{30}H_{48}O_2$	Olibanum	289	+115	Methyl ester, 214
Echinocystic acid	$C_{30}H_{48}O_4$	<i>Echinocystis fabacea</i>	305–12	+35 <sup>b,c</sup>	Methyl ester, 215
Erythrodiol	$C_{30}H_{50}O_2$	<i>Erythroxylon novogranatense</i>	232	+75	Diacetate, 188
Germanicol	$C_{30}H_{50}O$	<i>Latuca virosa</i>	177	+6	Acetate, 276
Gummosogenin	$C_{30}H_{48}O_3$	<i>Machaerocereus gummosus</i>	252	+28	Diacetate, 221
Glycyrrhetic acid	$C_{30}H_{46}O_4$	Liquorice root	300	+156	Methyl ester, 253
Gypsogenin	$C_{30}H_{46}O_4$	<i>Gypsophila</i> spp.	274	+91 <sup>b</sup>	Methyl ester, 192
Hederagenin	$C_{30}H_{48}O_4$	Soapnuts ( <i>Sapindus</i> spp.)	334	+76	Diacetate, 174
Icterogenin	$C_{30}H_{52}O_6$	<i>Lippia rehmanni</i> Pax.	240	+108	Methyl ester benzoate, 160
Longispinogenin	$C_{30}H_{50}O_3$	<i>Lemaireocereus longispinus</i>	240	+53	Triacetate, 221
Macheric acid	$C_{30}H_{48}O_4$	<i>Machaerocereus gummosus</i>	312	+20	Methyl ester, 198
Maniladiol	$C_{30}H_{50}O_2$	Manila elemi resin	221	+68	Diacetate, 194
Morolic acid	$C_{30}H_{48}O_3$	<i>Mora excelsa</i> Benth.	273	+32	Methyl ester, 229
Oleanolic acid	$C_{30}H_{48}O_3$	Clove buds	310	+78	Methyl ester, 201
Quillaic acid	$C_{30}H_{46}O_6$	Quillaja bark	293	+56 <sup>d</sup>	Methyl ester, 222
Rehmannic acid	$C_{30}H_{52}O_6$	<i>Lippia rehmanni</i> Pax.	300	+84	Oxime, 272
Siaresinolic acid	$C_{30}H_{48}O_4$	Siamese gum benzoin	292	+39	Methyl ester, 181
Sumaresinolic acid	$C_{30}H_{48}O_4$	Sumatra gum benzoin	299	+54	Methyl ester, 221
Taraxerol (skimmol)	$C_{30}H_{50}O$	<i>Skimmia japonica</i>	270	+8 (acetate)	Acetate, 297
<i>α-Amyrin Group</i>					
Asiatic acid	$C_{30}H_{48}O_5$	<i>Centella asiatica</i>	240	+52°	Methyl ester, 225
α-Amyrin	$C_{30}H_{50}O$	Manila elemi resin	186	+84	Acetate, 225
Brein	$C_{30}H_{50}O_2$	Manila elemi resin	218	+65	Diacetate, 196

TABLE II. Triterpenoid Sapogenins (Concluded).

Sapogenin	Formula	Source	M.p., °C.	$[\alpha]_D^{25}$ <sup>a</sup>	M.p. of derivative, °C.
$\beta$ -Boswellie acid	C <sub>30</sub> H <sub>48</sub> O <sub>3</sub>	Olibanum	240	+119	Methyl ester, 196
Phyllanthol	C <sub>30</sub> H <sub>50</sub> O	<i>Phyllanthus engleri</i> Pax.	226	+43	Acetate, 260
Ursolic acid	C <sub>30</sub> H <sub>48</sub> O <sub>3</sub>	Wax of leaves and fruits, e.g. bilberry	288	+70	Methyl ester, 171
Uvaol	C <sub>30</sub> H <sub>50</sub> O <sub>2</sub>	<i>Crataegus cuneata</i>	232	—	Diacetate, 159
<i>Lupeol-Betulin Group</i>					
Allobetulin	C <sub>30</sub> H <sub>50</sub> O <sub>2</sub>	German lignite	265	+48	Acetate, 281
Betulin	C <sub>30</sub> H <sub>50</sub> O <sub>2</sub>	<i>Betula alba</i>	261	+15	Diacetate, 223
Betulinic acid	C <sub>30</sub> H <sub>48</sub> O <sub>3</sub>	<i>Cornus florida</i>	318	+8 <sup>d</sup>	Methyl ester, 225
Lupeol	C <sub>30</sub> H <sub>50</sub> O	Sheanut fat, <i>Viscum</i> <i>album</i> , etc.	215	+27	Acetate, 218
<i>Taraxasterol Group</i>					
Taraxasterol	C <sub>30</sub> H <sub>50</sub> O	Dandelion ( <i>Tarax-</i> <i>acum officinale</i> )	221	+96	Acetate, 252
Pseudotaraxasterol (heterolupeol)	C <sub>30</sub> H <sub>50</sub> O	Dandelion	200	+47	Acetate, 235

<sup>a</sup> Rotations in chloroform unless otherwise specified.<sup>b</sup>  $[\alpha]_{5461}$ .<sup>c</sup> In ethyl alcohol.<sup>d</sup> In pyridine.<sup>e</sup> Methyl ester in ethyl alcohol.

### Acyclic Hydrocarbons

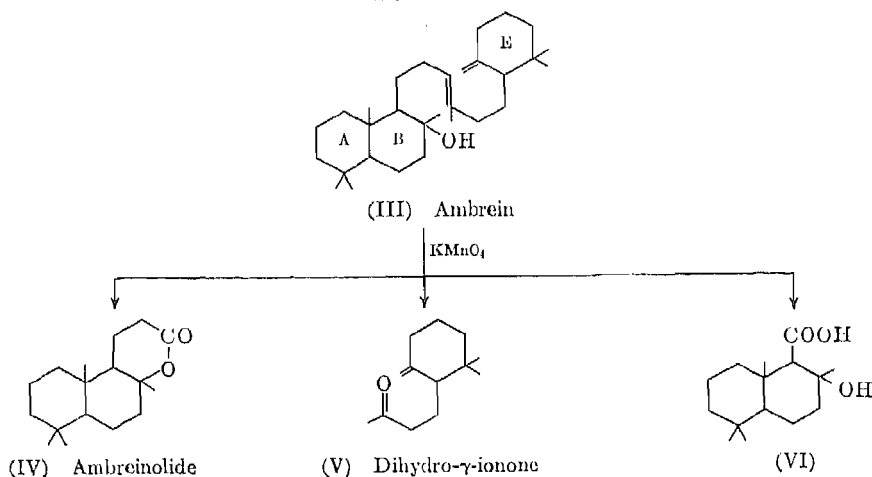
**Squalene** (II) contains six ethylenic linkages which, it has been shown, are all trans. It forms a hexahydrochloride, but the hydrocarbon regenerated from it does not appear to be identical with squalene, owing to double bond migration. Squalene has been synthesized by the condensation of two molecules of farnesyl bromide,  $(\text{CH}_3)_2\text{C}=\text{CHCH}_2\text{CH}_2\text{C}(\text{CH}_3)=\text{CHCH}_2\text{CH}_2\text{C}(\text{CH}_3)=\text{CHCH}_2\text{Br}$  (see p. 748).

Considerable interest has been aroused with regard to the role of squalene in the biosynthesis of cholesterol (see Vol. 12, p. 921). Thus, although squalene is poorly absorbed, the feeding of radioactive squalene to rats permitted the recovery of 8% of the activity in body cholesterol. The manner in which squalene cyclizes has been proposed and confirmation found in the distribution of the activity in biosynthesized active cholesterol. Squalene is a normal constituent of human sebum, ear wax, and hair fat. Squalene distilled from the liver oil of the basking shark and said to be 90–95% pure has recently been put on the market.

### Tricyclic Alcohol

**Ambrein** (III) is a tertiary alcohol. By oxidation with potassium permanganate it yields a lactone *ambreinolide* (IV) together with *dihydro- $\gamma$ -ionone* (V) (Scheme I). Both these compounds have been synthesized. A by-product from this oxidation is the compound (VI), of importance in the relationship to rings A and B of oleanolic acid (see p. 766).

SCHEME 1



### Pentacyclic Compounds

This class can be divided into four groups: (1) the  $\beta$ -amyrin group, (2) the  $\alpha$ -amyrin group, (3) the lupeol-betulin group, and (4) the taraxasterol group.

Apart from description by reference to the parent alcohol, for example,  $\beta$ -amyrin and the hydrocarbon derived therefrom, the term *oleanane* is used as a trival name for the saturated  $\text{C}_{30}$  skeleton of the  $\beta$ -amyrin series. On this basis oleanolic acid is olean-12-en-3 $\beta$ -olic acid, and  $\beta$ -amyrin is olean-12-en-3 $\beta$ -ol. A similar scheme obtains in the  $\alpha$ -amyrin group (*ursane*), the lupeol group (*lupane*), and the taraxasterol group (*taraxastane*).

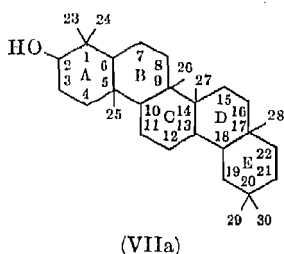
The naturally occurring pentacyclic triterpenoids are highly crystalline compounds with a tendency to form mixed crystals. In general, they are oxygenated at C(3), and in most cases the function is a  $\beta$ -hydroxyl group, which is easily acylated. In a few cases an  $\alpha$ -hydroxyl (as in  $\beta$ -boswellic acid) or a ketonic group (as in icterogenin) may occur. The nucleus may be saturated or, much more probably, contain one or even more ethylenic linkages: oxygen functions have been encountered in a large number of the possible positions in the nucleus of the  $\beta$ -amyrin group though not in the other smaller groups. A carboxyl group frequently occurs at C(17). Interrelationship between members of the first, third, and fourth groups has been established but not between the whole nucleus of a member of these and the second group. The first two groups appear to be stereochemically identical in all groups.

Apart from direct information, such as is obtained, for instance, by dehydrogenation (in this class of limited use), the methods of approach have frequently been twofold. The triterpenoid can be transformed into some compound of known structure, as was largely the case, for example, with lupeol and morolic acid, or it can be broken down into simpler, ultimately recognizable, fragments. This has generally been the procedure with the parents of a group of triterpenoids (for example, oleanolic acid) or with compounds not so far directly related to a group (for example, quinovic acid).

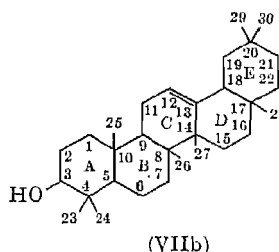
### THE $\beta$ -AMYRIN GROUP

$\beta$ -Amyrin, the parent alcohol of this group, has the constitution (VII). This was formerly written as (VIIa) (the double bond at 12(13) is not shown) but has been

recently altered to (VIIb) in accordance with the demonstrated stereochemical relationship with the steroids.



(VIIa)

 $\beta$ -Amyrin

(VIIb)

Application of the dehydrogenative technique (as used on the di- and sesquiterpenoids) is of limited value because the molecule has a tendency to break into two fragments. A number of methylated benzene and naphthalene derivatives have been isolated such as 1,2,7-trimethylnaphthalene (sapotalene), although products of the entire skeleton have been found in 1,8-dimethylpicene and 1,8-dimethylpicen-2-ol.

The double bond at 12(13) in the  $\beta$ -amyryn group is entirely resistant to hydrogenation, although it gives a yellow color with tetranitromethane and may be detected in the near-ultraviolet. It is, however, attacked by peroxy acids whereby a 12-ketone may be obtained. The carbonyl group in this position is removable by the Wolff-Kishner procedure (see Vol. 8, p. 119). Chromic acid oxidation of the nucleus yields, by allylic oxidation under quite mild conditions, the 11-ketone, as shown by the absorption maximum at 249  $\mu$ . Members of the group possessing a carboxyl group at C(17) (as in oleanolic acid) readily lactonize onto the double bond under acidic conditions to give an equilibrium mixture (obtainable from the acid or lactone); with oleanolic acid, this consists of about 25% lactone:75% acid. With bromine, these acids give, irreversibly, bromo lactones convertible back into the acids by treatment with zinc and acetic acid.

The ubiquitous hydroxyl group at C(3) is easily acylable, and the derived ketone forms the usual derivatives. Wolff-Kishner reduction converts the ketone to the hydrocarbon. Treatment of the alcohol (VIII) itself with phosphorus pentachloride results in a retropinacolic rearrangement to give a contracted ring A (IX). The resultant isopropylidene product with osmium tetroxide followed by lead tetraacetate or periodic acid gives a norketone and acetone. The double bond may be also be ozonized.



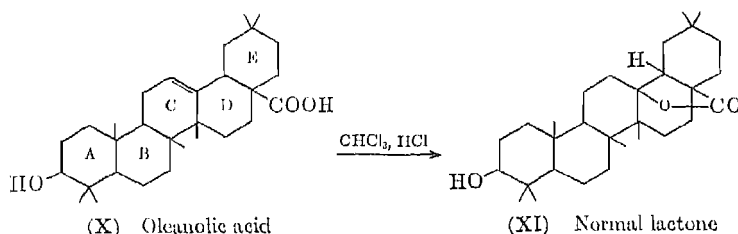
(VIII)

(IX)

This series of reactions has been used for degradative purposes in all four groups of the pentacyclic triterpenoids and also in the tetracyclic series. It requires that the alcohol be in the equatorial (3 $\beta$ ) configuration; similar treatment of the epimeric alcohol leads to the formation of, largely, compounds with a double bond at C(2).

**Oleanolic acid** (X) differs from  $\beta$ -amyryn in having a carboxyl group at C(17). It has been of particular use in the elucidation of the structure of the  $\beta$ -amyryn skeleton. After breaking of the C(11)-C(12) bond, by oxidative cleavage, pyrolysis results in

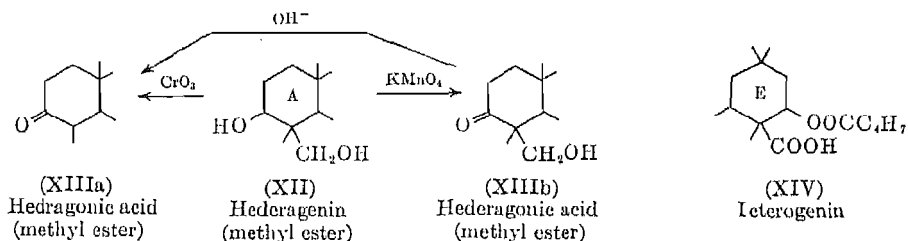
two portions, one containing the A and B rings (related to the acid (VI) from ambrein) and the other the D and E rings.



Treatment of oleanolic acid with chloroformic hydrogen chloride gives the *normal lactone* (XI), while treatment with reagents of a greater proton-donating power, such as hydrobromic acid/acetic acid, yields the 18-isolactone. This reaction, unlike the formation of the normal lactone, is not reversible. Allylic oxidation yields the 11-ketone, which can be reconverted to the original system on catalytic reduction. The same is true of the 18-iso series. Treatment of the 11-ketone with alkali also isomerizes at C(18).

Reduction of oleanolic acid with lithium aluminum hydride gives erythrodiol (olean-12-en-3,28-diol), while reduction of the acid chloride (Rosenmund) to the aldehyde and Wolff-Kishner reduction yield  $\beta$ -amyrin.

**Hederagenin** (23-hydroxyoleanolic acid) (XII), like oleanolic acid, can be converted into an 18-iso series with acid reagents. Oxidation of hederagenin methyl ester with chromic acid yields, via an intermediate  $\beta$ -keto acid, *methyl hederagonate* (XIIIa). Oxidation with potassium permanganate in acetone yields the 3-ketone (*methyl hederagonate*, XIIIb), leaving the primary alcohol untouched. Compounds of the type of methyl hederagonate (as icterogenin, asiatic acid) readily lose formaldehyde on treatment with base, by a retroaldol condensation, to give the norketones (5), such as methyl hederagonate.



The aldehyde corresponding to hederagenin is **gypsogenin**. On Wolff-Kishner reduction it yields oleanolic acid.

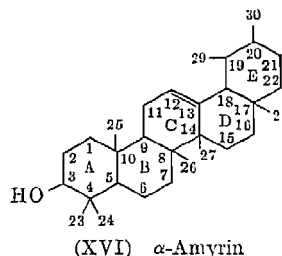
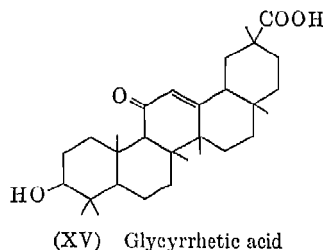
**Echinocystic acid** is the 16-hydroxy derivative of oleanolic acid, into which it can be converted by dehydration of the 16-hydroxyl with methanesulfonyl chloride and pyridine, followed by saturation of the ethylenic linkage so formed (17).

Other 16-oxygenated triterpenoids found in nature are **gummosogenin** (3 $\beta$ ,16 $\beta$ -dihydroxyolean-12-en-28-al) and **longispinogenin** (olean-12-en-3 $\beta$ ,16 $\beta$ ,28-triol), both of which occur in cacti (7a).

**Icterogenin** is the 4-*epi*-22 $\beta$ -angeloyloxy derivative (XIV) of hederagonic acid (XIIIb). On treatment with alkali, formaldehyde is liberated by dealdolization. Icterogenin is biologically active, being responsible for *geel-dikkop* (yellow thick head)

in sheep (5). The related **rehmannic acid** (22 $\beta$ -angeloyloxyoleanonic acid) is inactive.

**Glycyrrhetic acid** (glycyrrhetic acid) (XV) is an  $\alpha,\beta$ -unsaturated keto acid which on catalytic hydrogenation yields a dihydro derivative isomeric with oleanolic acid.

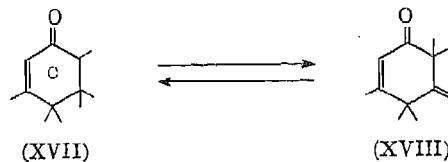


**Siaresinolic acid** is 19-hydroxyoleanolic acid. The axial hydroxyl group at C(19) is very hindered and cannot be acylated under conditions which readily acylate the hydroxyl at C(3). Oxidation gives a ketone which is isomerized on treatment with alkali to an 18-iso compound. Saturation of the double bond at 12(13) by conversion to the 12-ketone and subsequent Wolff-Kishner, followed by dehydration of the 19-hydroxyl, yields morolic acid.

**Morolic acid** (3) differs from  $\beta$ -amyrin in the position of the double bond, which is here at 18(19). It is decarboxylated smoothly at the melting point to give 28-noroleanon-3 $\beta$ -ol in almost quantitative yield. Conversion of the carboxyl group into methyl yields *germanicol*. Morolic acid has also been related to the lupeol-betulin group (12).

#### THE $\alpha$ -AMYRIN GROUP

The reactions of this group of compounds as a whole parallel those of the  $\beta$ -series. However, there are some important differences in behavior. The ethylenic linkage is far more hindered but is attacked by ozone or peroxyacetic acid, yielding an oxide. The oxide is rearranged on treatment with acid to give the 12-ketone (20). This ketone exhibits a greater degree of hindrance than that of the  $\beta$ -series, as is indicated by its failure to form ketonic derivatives. This property is accommodated by the formulation (XVI) for  $\alpha$ -amyrin. Treatment of  $\alpha$ -amyrin benzoate oxide with bromine in acetic acid converts it into the 11-bromo 12-ketone, which spontaneously dehydrobrominates to give *iso- $\alpha$ -amyrenonyl benzoate* (XVII). This with selenium dioxide yields (XVIII) with concomitant methyl migration. Hydrogenation regenerates (XVII).

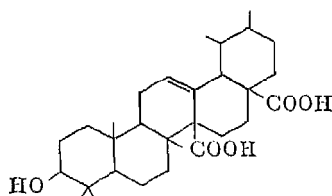


**Ursolic acid**, the 17-carboxylated compound of  $\alpha$ -amyrin, in distinction from oleanolic acid, on treatment with bromine does not yield a bromo lactone, but with chloroformic hydrogen chloride gives an equilibrium mixture containing about 10%

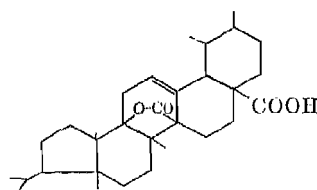
of lactone. It does not, however, show any tendency to isomerize on treatment with more powerful acid reagents and the derived 11-ketone, unlike the oleanolic acid derivative, is not isomerized by base (15).

**Phyllanthol** (13,27-cycloursan-3 $\beta$ -ol) (7) is a hexacarboecyclic triterpenoid containing a cyclopropane ring. Treatment with hydrogen chloride in chloroform or with hydrochloric acid in acetic acid yields  $\alpha$ -amyrin.

**Quinovic acid** most probably has the constitution (XIX) and is thus a member of the  $\alpha$ -amyrin series, although no direct relationship has yet been demonstrated (6,11). It is easily decarboxylated at the melting point, in keeping with its formulation as a  $\beta,\gamma$ -unsaturated acid, to give pyroquinovic acid. Treatment of quinovic acid under strong acid conditions yields **novic acid** (XX), in which there has been retropinacolic ring contraction and methyl migration with the formation of a  $\gamma$ -lactone.

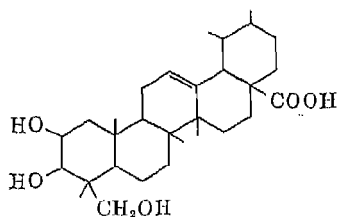


(XIX) Quinovic acid

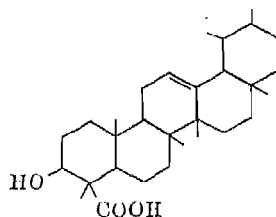


(XX) Novic acid

**Asiatic acid** (XXI) has three hydroxyl groups, two of which are contained in an  $\alpha$ -glycol system (18). Chromic acid oxidation of the methyl ester followed by Clemmensen reduction and conversion of the carboxyl to methyl yields 23-nor- $\alpha$ -amyrin, which has also been obtained from  $\beta$ -boswellic acid (XXII).



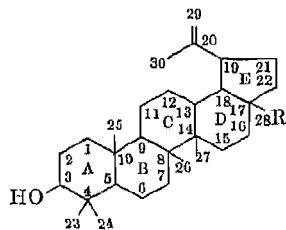
(XXI) Asiatic acid

(XXII)  $\beta$ -Boswellic acid

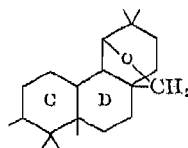
#### THE LUPEOL-BETULIN GROUP

In this group ring E is five-membered and substituted by an isopropenyl group. The double bond is easily hydrogenated.

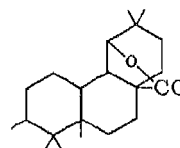
**Lupeol.** This alcohol (XXIII, R = CH<sub>3</sub>) is easily converted into the 3-ketone, *lupenone*, and thence to the hydrocarbon  $\alpha$ -*lupene*. Treatment of  $\alpha$ -lupene with acid



(XXIII)



(XXIV)



(XXV)



induces an extensive rearrangement with the production of olean-13(18)-ene, which is also obtained from  $\beta$ -amyrene (the hydrocarbon derived from  $\beta$ -amyrin) on acid isomerization. Similarly lupenone has been converted into the related ketone, olean-13(18)-en-3-one.

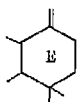
**Betulin** (XXIII,  $R = CH_2OH$ ) can be obtained from betulinic acid by reduction with lithium aluminum hydride. Oxidation and Wolff-Kishner reduction yield lupeol. With formic acid it undergoes expansion of ring E, in a manner similar to lupeol, the primary alcohol group then closing to give *allobetulin* (XXIV). Oxidation of allobetulin yields a lactone, *28-oxoallobetulin* (XXV).

**Betulinic acid** (XXIII,  $R = COOH$ ) as the methyl ester rearranges and cyclizes on oxidation under acid conditions to give a lactone which is the 3-ketonic derivative of (XXV). Reduction of this lactone with lithium aluminum hydride affords a triol, which is also obtained from siarasinolic acid (see p. 767) by oxidation at C(19), inversion at C(18), and reduction. This triol after acetylation and dehydration at C(19) gives moradiol diacetate, which can be obtained from morolic acid by reduction and acetylation.

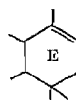
#### THE TARAXASTEROL GROUP

The members of this group have a six-membered ring E, a  $3\beta$ -hydroxyl group, and contain a reactive double bond.

**Taraxasterol** (XXVI) has an exocyclic ethylenic linkage which is isomerized by sulfuric acid in ethanolic benzene to **pseudotaraxasterol** (heterolupeol) (XXVII), in which the double bond has moved into the ring. Pseudotaraxasterol is also formed from lupeol (XXIII,  $R = CH_3$ ) by treatment with boiling formic acid, while under more vigorous conditions the double bond moves into the 13(18)-position. These experiments establish the nature of all but the last ring in this series; recent degradative work has fixed the position of unsaturation (13).



(XXVI) Taraxasterol



(XXVII) Pseudotaraxasterol

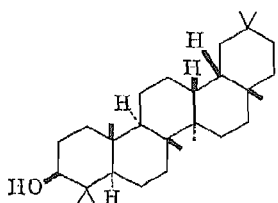
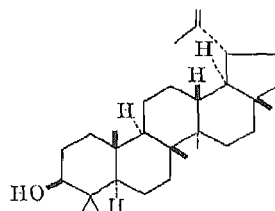
Hydrogenation of the reactive double bonds in the derived hydrocarbons yields, in both cases, the saturated taraxastane, which is the parent skeleton for nomenclature. Taraxastene is thus taraxast-20(30)-ene.

#### Stereochemistry

*The  $\beta$ -Amyrin Group.* Rings A and B in all the pentacyclic triterpenoids are fused trans. This has been established by the relationship of degradation products of these compounds with those of the first two rings of the diterpenoids (see p. 754), in which the ring junction has been shown to be trans. If the C(5)-methyl group in triterpenoids is considered to be above the plane of the paper (that is,  $\beta$ ), the hydroxyl group at C(3) is also  $\beta$  (equatorial). (See *Stereochemistry (organic)*, Vol. 12, p. 858; *Sterols and steroids*.) This statement is supported by the ease of acylation (2) and of hydrolysis of esters at this point, and by the fact that oxidation to the ketone and reduction with sodium and alcohol (which yield the more stable equatorial alcohol) give back the original alcohol. Further evidence is obtained from the retropinacolic

ring contraction (see p. 765), which requires that the C—O bond and the C(4)-C(5) bond should be in one plane.

As already mentioned, the configuration at C(18) is unstable. In particular, the inversion at C(18) and not at C(10) in the 11-ketones testifies to the stability of the configuration at C(10) and the reverse at C(18). Rings D/E are therefore *cis*-fused. Arguing, then, from the known stabilities of ring fusions in perhydrophenanthrenes, it follows that ring C is a "chair," and from this and other evidence it can be demonstrated that the hydrogen at C(10) is *trans* to the carboxyl group in oleanolic acid. This must be axial to account for its ready lactonization. Since D/E is *cis* and *syn*, the hydrogen at C(13) (in the more stable arrangement) being *cis* to the carboxyl, it follows that the C/D junction must therefore be *trans*. The possibilities remaining for rings A, B, and C are therefore *trans:syn:cis* and *trans:anti:trans* (4). This second possibility has been supported on the basis of molecular rotations which have also indicated that the absolute configurations (14) of the triterpenoids are the same as the steroids in rings A and B. The final stereochemistry of  $\beta$ -amyranol as (XXVIII) has been demonstrated by x-ray investigations of methyl oleanolate iodoacetate.

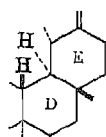
(XXVIII)  $\beta$ -Amyranol

(XXIX) Lupeol

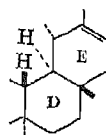
*The  $\alpha$ -Amyrin Group.* The stereochemistry in this group has not been rigidly established beyond that of rings A and B, which is identical with that of  $\beta$ -amyrin.

*The Lupeol-Betulin Group.* The relationship of lupeol to  $\beta$ -amyrin has fixed the stereochemistry as far as the centers C(3), C(5), C(8), C(9), C(10), C(14), and C(17) are concerned (12), and the configuration at C(13) is that of morolic acid. The preparation of the triol from both oxallobetulin and siarasinolic acid after the latter's inversion at C(18) indicates that in this series the D/E junction must be *trans*. Similarly, treatment of lupeol acetate with hydrogen chloride gives a chloro compound, which on reduction with Raney nickel yields 18-iso- $\beta$ -amyranol, a compound derived from  $\beta$ -amyrin and with a *trans* D/E junction. The isopropenyl group is *trans* to the function at C(17). The stereochemistry of lupeol is thus as shown in the formulation (XXIX).

*The Taraxasterol Group.* The stereochemistry of rings A, B, C, and D in taraxasterol and pseudotaraxasterol is identical with that of  $\beta$ -amyranol and lupanol. However, since allobetulin may be converted through heterobetulin to pseudotaraxasterol, rings D and E must be *trans*-fused, as in the lupeol-betulin series. The methyl group at C(19) is in the  $\alpha$  (equatorial) configuration but is unusual in that the



(XXX) Taraxasterol



(XXXI) Pseudotaraxasterol

equatorial position is less stable than the  $\beta$  (axial) position. The stereochemistry is represented by (XXX) and (XXXI), respectively.

### Bibliography

- (1) Barton, D. H. R., "Triterpenoids," in Rodd, *Chemistry of the Carbon Compounds*, Elsevier, Houston, Tex., and Amsterdam, 1953, Vol. IIB, ch. XVI; "The Chemistry of the Triterpenoids," in Cook, *Progress in Organic Chemistry*, Butterworths, London, 1953, Vol. II, pp. 67-103.
- (2) Barton, D. H. R., *Experientia*, **6**, 316 (1950); *J. Chem. Soc.*, **1953**, 1027.
- (3) Barton, D. H. R., and Brooks, C. J. W., *J. Chem. Soc.*, **1951**, 257.
- (4) Barton, D. H. R., and Holness, N. J., *J. Chem. Soc.*, **1952**, 78.
- (5) Barton, D. H. R., and Mayo, P. de, *J. Chem. Soc.*, **1954**, 887, 900.
- (6) Barton, D. H. R., and Mayo, P. de, *J. Chem. Soc.*, **1953**, 3111.
- (7) Barton, D. H. R., Page, J. E., and Warnhoff, E. W., *Chemistry & Industry*, **1954**, 220.
- (7a) Djerassi, C., Geller, L. E., and Lemin, A. J., *Chemistry & Industry*, **1954**, 161.
- (8) *Elsevier's Encyclopaedia*, Vol. 14, ch. IV, 1940, and Supplement, Part II, 1952.
- (9) Groen, J., *et al.*, *J. Clin. Invest.*, **31**, 87 (1952).
- (10) Jeger, O., *Fortschr. Chem. org. Naturstoffe*, **7**, 1 (1950).
- (11) Jeger, O., Ruzicka, L., *et al.*, *Helv. Chim. Acta*, **34**, 244 (1951).
- (12) Jones, E. R. H., *et al.*, *J. Chem. Soc.*, **1951**, 450, 2696.
- (13) Jones, E. R. H., *et al.*, *J. Chem. Soc.*, **1954**, 1902, 1905.
- (14) Klyne, W., *J. Chem. Soc.*, **1952**, 2916.
- (15) Meisels, A., Jeger, O., and Ruzicka, L., *Helv. Chim. Acta*, **32**, 1075 (1949).
- (16) *Nature*, **155**, 601 (1945).
- (17) Noller, C. R., *et al.*, *J. Am. Chem. Soc.*, **66**, 1267 (1944) and previous papers in this series.
- (18) Polonsky, J., *Compt. rend.*, **233**, 671 (1951) and previous parts of this series; *Bull. soc. chim. France*, **1952**, 649, 1015.
- (19) Ruzicka, L., and Hofmann, K., *Helv. Chim. Acta*, **19**, 126 (1936).
- (20) Spring, F. S., *et al.*, *J. Chem. Soc.*, **1939**, 1079; **1941**, 319; **1951**, 935.
- (21) Woodward, R. B., Barton, D. H. R., *et al.*, *J. Am. Chem. Soc.*, **76**, 2852 (1954).

P. DE MAYO

**TERPHENYL**,  $C_{18}H_{14}$ . See *Diphenyl and terphenyls*, Vol. 5, p. 148.

**1,8-TERPIN, TERPINOL**,  $C_{10}H_{20}O_2$ ; **TERPIN HYDRATE**,  $C_{10}H_{20}O_2 \cdot H_2O$ . See *Emetics and expectorants*, Vol. 5, p. 684; *Terpenes (mono-, cyclic)*.

$\alpha$ -,  $\beta$ -, and  $\gamma$ -**TERPINENES**,  $C_{10}H_{16}$ . See *Terpenes (mono-, cyclic)*.

$\alpha$ -,  $\beta$ -, and  $\gamma$ -**TERPINEOLS**,  $C_{10}H_{17}OH$ . See *Perfumes (synthetics and isolates)*, Vol. 10, p. 18; *Terpenes (mono-, cyclic)*.

**TERPINOLENE**,  $C_{10}H_{16}$ . See *Terpenes (mono-, cyclic)*.

**TERRAZZO**. See *Cement products*, Vol. 3, p. 482.

**TESTOSTERONE**,  $C_{19}H_{28}O_2$ . See *Hormones (sex)*, Vol. 7, p. 531.

**TETRACAINE HYDROCHLORIDE**,  $p-(CH_3)_2NCH_2CH_2OOC C_6H_4NH(CH_2)_3CH_3 \cdot HCl$ . See *Anesthetics*, Vol. 1, p. 908.

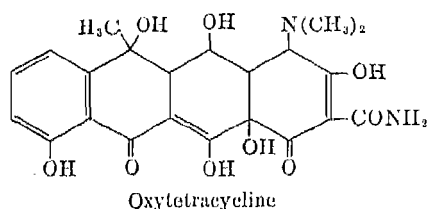
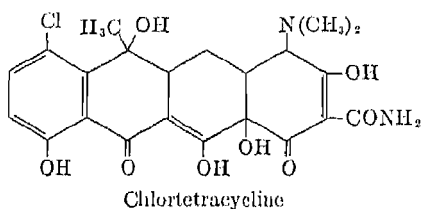
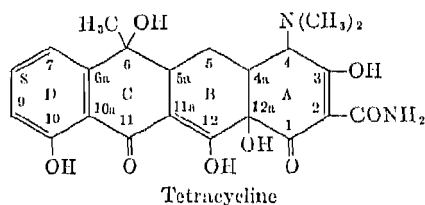
**TETRACENE**,  $ONHNHC(:NH)N:NNHNHC(:NH)NH_2$ . See *Explosives (high)*, Vol. 6, p. 15.

**TETRACHLOROETHANES**,  $C_2H_2Cl_4$ . See *Chlorine compounds, organic*, Vol. 3, p. 767.

## TETRACYCLINES

Chlortetracycline.....	p. 774
Oxytetracycline.....	790
Tetracycline.....	803

The tetracyclines are a group of crystalline antibiotics that possess a common hydronaphthacene skeleton. Tetracycline (Achromycin, Tetracin, etc.) (11), although the last of the drugs to be described, can be considered the parent compound of the group and is structurally 4-dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,-12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacene-carboxamide. Chlortetracycline (Aureomycin) is the 7-chloro, and oxytetracycline (Terramycin) the 5-hydroxy derivative of tetracycline. See also *Antibiotics*; *Streptomyces antibiotics*.



**Properties.** As a group, the tetracyclines are soluble in glycol ethers, pyridine and dilute acid and alkali; slightly soluble in water and alcohols; and insoluble in ether and petroleum ether. The characteristics of the ultraviolet spectra of tetracycline in acidic and basic solutions are very similar to those of the corresponding spectra (9) for oxytetracycline. The spectra of tetracycline and chlortetracycline (3) in acid solution are also very similar (11).

Chemically, the three compounds resemble one another in that they all form salts easily with both acids and bases. The tetracyclines undergo series of characteristic reactions in acids and bases, which will be discussed under the individual sections. Despite the close structural relationships of the tetracyclines, their chemistry differs in many respects.

**Preparation.** All three antibiotics may be manufactured by fermentation using species of *Streptomyces*, and, in addition, tetracycline is also manufactured by the hydrogenolysis of chlortetracycline.

**Microbiology.** Tetracycline possesses an activity comparable to oxytetracycline and chlortetracycline. The antibacterial action of all three tetracyclines was tested *in vitro* against strains of 12 varieties of bacteria freshly isolated from patients. Certain strains of *Enterococcus*, *Staphylococcus aureus* (*Micrococcus pyogenes* var. *aureus*) and *Aerobacter aerogenes* and most of the strains of *Proteus* and *Pseudomonas* were found to be resistant while other strains of the same species were sensitive to a moderate or high

degree (14). In a study of 338 strains of coagulase-positive staphylococci, the three drugs exhibited varying degrees of activity (12). No significant differences in the activities of the tetracyclines have been demonstrated against either Gram-positive or -negative organisms (5,8), even when the three drugs were studied with agar streak, agar diffusion, and turbidimetric methods (2,5).

The tetracyclines were evaluated, and the activities of the individual antibiotics compared, in experimental infections with Gram-positive and -negative bacteria in animals (5,7,8). There were no significant differences in activity among the three antibiotics except in infections of *Pasteurella*, *Klebsiella*, and *Mycobacterium* in which either oxytetracycline or chlortetracycline exhibited greater effectiveness (7).

In those studies which have been reported, there is complete cross resistance between the three analogs *in vitro* (5,6,13,14). The increase in resistance to the tetracyclines by transfer in media containing increasing concentrations of the drug is gained slowly in a gradual, stepwise fashion comparable to that of penicillin (11a). The artificial increase of resistance of certain microorganisms to one drug coincides with a similar increase of resistance to the other two antibiotics (13).

**Pharmacology.** The tetracyclines may be administered orally, intravenously, and intramuscularly. Each drug is readily absorbed from the gastrointestinal tract and subsequently appears in the various body fluids. A large part of the drug not absorbed is recovered in the stool. The antibiotics appear in the urine in fairly high concentrations during the first two hours after administration and maintain maximum concentrations for 6 to 12 hours. About 10–20% of the drug is recovered in the urine during the first 12 hours, but the amount excreted during the second 12-hour period varies considerably (14).

The tetracyclines are drugs of low toxicity. They appear to cause an accumulation of fat in the liver of rats. However, in this respect neither of the nonchlorinated analogs was found to be as active as the chlorine-containing antibiotic (10). The side effects associated with the administration of any one of the antibiotics are generally of the nature of minor digestive upsets or diarrhea; however, tetracycline has been reported (5a) to have a significantly lower incidence of gastrointestinal side effects.

A study of the mechanism of action of the three antibiotics has shown (3) that the tetracyclines uncouple the oxidative-phosphorylation and inhibit the oxidation of octanoate in liver mitochondrial preparations. The effect appears to be greatest at low concentrations of magnesium ions.

**Specifications, Assay, and Uses.** Tetracycline and chlortetracycline are certifiable antibiotics, and each batch must meet the specifications of the Food and Drug Administration before shipment in interstate commerce. Oxytetracycline must pass rigid tests set up by the manufacturer before being offered for sale.

Among other methods, the three related antibiotics can be differentiated by infrared spectra and paper chromatography. In the paper chromatographic method, the filter paper is treated with pH 3.0 phosphate buffer and the chromatogram is developed with ethyl acetate saturated with water (1). The position of the antibiotic on the papergram can be determined by bioautograph or by ultraviolet scanning. The papergram may also be developed with *n*-butyl alcohol, *n*-amyl acetate, etc. (2).

Although tetracycline, the newest of the tetracyclines, has not been fully evaluated, the clinical indications for the three related antibiotics appear to be similar (11a,11b). These antibiotics are prescribed for those patients who may develop an anaphylactic reaction due to certain allergic manifestations to penicillin.

## Bibliography for Tetracyclines

- (1) Bird, H. L., Jr., and Pugh, C. T., *Antibiotics & Chemotherapy*, **4**, 750 (1954).
- (2) Bohonos, N., Dornbush, A. C., Feldman, J. I., Martin, J. H., Peleak, E., and Williams, J. H., *Antibiotics Ann.*, **1953-54**, 49.
- (3) Brody, T. M., and Hurwitz, R., *Antibiotics & Chemotherapy*, **4**, 864 (1954).
- (4) Broschard, R. W., Dornbush, A. C., Gordon, S., Hutchings, B. L., Kohler, A. R., Krupka, G., Kushner, S., Lefemine, D. V., and Pidaaks, C., *Science*, **109**, 199 (1949).
- (5) English, A. R., P'an, S. Y., McBride, J., Gardloeki, J. F., Van Halsema, G., and Wright, W. A., *Antibiotics & Chemotherapy*, **4**, 411 (1954).
- (5a) Finland, M., et al., *J. Am. Med. Assoc.*, **154**, 561 (1954).
- (6) Finland, M., Purcell, E. M., Wright, S. S., Love, B. D., Jr., Mou, T. W., and Kass, E. H., *J. Am. Med. Assoc.*, **154**, 561 (1954).
- (7) Kiser, J. S., deMello, G. C., Lindh, E. H., Malone, L. L., Popken, F., Schurr, A., and Waters, M. K., *Antibiotics Ann.*, **1953-54**, 56.
- (8) Minieri, P. P., Firman, M. C., Mistretta, A. G., Abbey, A., Bricker, C. E., Rigler, N. E., and Sokol, H., *Antibiotics Ann.*, **1953-54**, 81.
- (9) Regna, P. P., Solomons, I. A., Murai, K., Timrock, A., Brunings, K. J., and Lazier, W. A., *J. Am. Chem. Soc.*, **73**, 4211 (1951).
- (10) Seto, J. T., and Lepper, M. H., *Antibiotics & Chemotherapy*, **4**, 666 (1954).
- (11) Stephens, C. R., Conover, L. H., Hochstein, F. A., Regna, P. P., Pilgrim, F. J., Brunings, K. J., and Woodward, R. B., *J. Am. Chem. Soc.*, **74**, 4976 (1952).
- (11a) Waddington, W. S., Bergy, G. G., Nielson, R. L., and Kirby, W. M. M., *Am. J. Med. Sci.*, **228**, 164 (1954).
- (11b) Welch, H., *Principles and Practice of Antibiotic Therapy*, Medical Encyclopedia, Inc., N.Y., 1954, chs. VIII, X, XI.
- (12) Welch, H., Randall, W. A., Reedy, R. J., and Oswald, E. J., *Antibiotics & Chemotherapy*, **4**, 741 (1954).
- (13) Wright, S. S., and Finland, M., *Proc. Soc. Exptl. Biol. Med.*, **85**, 40 (1954).
- (14) Wright, S. S., Purcell, E. M., Love, B. D., Jr., Mou, T. W., Kass, E. H., and Finland, M., *Antibiotics Ann.*, **1953-54**, 92.

PETER P. REGNA

## CHLORTETRACYCLINE

Chlortetracycline (Aureomycin, U.S.P. XIV, N.N.R.),  $C_{22}H_{23}ClN_2O_8$  (see p. 772), introduced in 1948, is produced by *Streptomyces aureofaciens*, isolated from a soil sample from a timothy field in Missouri. The antibiotic was rapidly recognized as an important and highly effective agent against a broad spectrum of infectious diseases. It was one of the first therapeutic antibiotics useful against rickettsiae and the psittacosis-lymphogranuloma viruses as well as bacterial infections caused by Gram-positive and Gram-negative bacteria. Chlortetracycline is commercially available as the free base and its hydrochloride. The constitution of this antibiotic has been established, only  $3\frac{3}{4}$  years elapsing from the time of the first chemical publication (4) to the announcement of the completed structure (21,27).

## Properties

**Physical Properties.** Chlortetracycline is a yellow, crystalline compound; m.p., 168-169°C. (uncorr.);  $[\alpha]_D^{23} = 274.9^\circ$  (methanol). It is very soluble in 2-ethoxyethanol, pyridine, dioxane, and 2-(2-ethoxyethoxy)ethanol; slightly soluble in methanol, ethyl alcohol, *n*-butyl alcohol, acetone, ethyl acetate, and benzene; soluble in water to the extent of about 0.55 mg./ml. at 25°C.; and insoluble in ether and

petroleum ether. The crystals are very small, acicular to bladed in habit, and have a refractive index parallel to elongation of slightly greater than 1.674 but not more than 1.694 (4,34). The ultraviolet absorption spectra of chlortetracycline at different pH values have been measured (17,24,34). When solutions of this antibiotic in 0.1 N HCl or water are refrigerated, there is no change in their absorption spectra over a period of a week or two, but a refrigerated alkaline solution shows a daily change in absorption. Acid solutions of the antibiotic, on standing at room temperature or heating, show pronounced changes in spectra (10). Treatment with acid at 100°C. has been used both for the colorimetric (16) and the ultraviolet (10) determination of chlortetracycline.

A characteristic infrared absorption spectrum is given by a sample mullied in hydrocarbon oil (34). The following absorption bands, at frequencies expressed in reciprocal centimeters, were obtained with the free base: 3,420, 3,050, 1,643, 1,609, 1,580, 1,523, 1,302, 1,231, 1,209, 1,121, 1,080, 1,050, 969, 943, 867, 844, 825, 805, 794, 788, 733, and 713. The monohydrochloride salt showed bands at: 3,295, 3,050, 1,665, 1,615, 1,575, 1,523, 1,310, 1,263, 1,225, 1,044, 1,009, 969, 863, 851, 840, 800, 770, and 698.

**Chemical Properties.** Chlortetracycline is 7-chloro-4-dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide (5). It is an amphoteric compound and forms salts with such bases as sodium and potassium hydroxides and with such acids as hydrochloric, sulfuric, phosphoric, and acetic. Precipitates are formed in aqueous solutions with picric acid, Reinecke's acid, and ammonium molybdate. The antibiotic is soluble in dilute acids but tends to precipitate from solution near neutrality. It decomposes when heated in strong acids or alkalies; basic solutions develop a fluorescence, the speed of this reaction greatly increasing with temperature. The maximum intensity is reached at pH 10-12.

*Chlortetracycline hydrochloride*, the form of chlortetracycline most extensively used by the medical profession, decomposes above 210°C.;  $[\alpha]_D^{25} = -240.5^\circ$  (0.5% in water). It is soluble in water, about 14 mg./ml. at 25°C.; soluble in methanol; and slightly soluble in ethyl alcohol and acetone. Crystals occur in tabular or equidimensional orthorhombic form, sometimes showing a rhomboid outline. There is no marked cleavage, and on breaking the crystals show a conchoidal fracture. Examination under the polarizing microscope shows the crystals to be biaxial with an optical angle of  $>60^\circ$ , optical sign negative. Crystallographic data have been obtained for chlortetracycline hydrochloride by several workers (8,9,18,34).

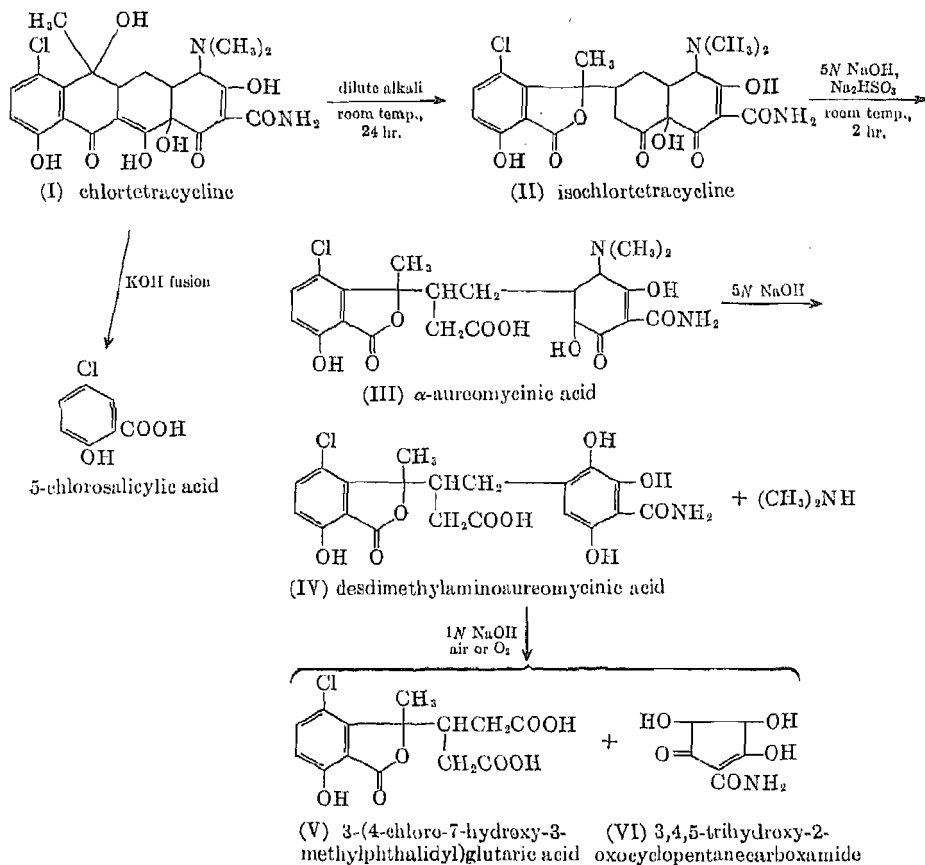
Apparent dissociation constants ( $pK'_a$ ) for chlortetracycline have been reported (17) to be 3.14, 7.33, and 9.24. The true dissociation constants ( $pK_a$ ) (0.005 M) have been given as 3.30 ( $\pm 0.02$ ), 7.44 ( $\pm 0.01$ ), and 9.27 ( $\pm 0.03$ ); the 3.30 value represents the ionization of cations, the others of anions (1).

Albert (1) reports the stability constants for the metal complexes of chlortetracycline to decrease as follows:  $Fe^{3+} > Cu^{2+} > Fe^{2+} > Co^{2+} > Zn^{2+} > Mn^{2+}$ . The copper complex was green in color, the ferrous and ferric complexes red, and the others yellow. Two patents (36,38) relate to the synthesis of complexes of the antibiotic, such as the borate, and those with the halides of Al, Co, Sn, Zn, B, Mg, Fe, and Ni. These complexes have solubility characteristics which render them of interest.

The known chemistry of chlortetracycline can be placed in three general classes of

reactions: hydrolysis, reduction, and oxidation. Structural determinations were largely based on the interpretation of the results of *alkaline degradation* (see Scheme 1)

SCHEME 1

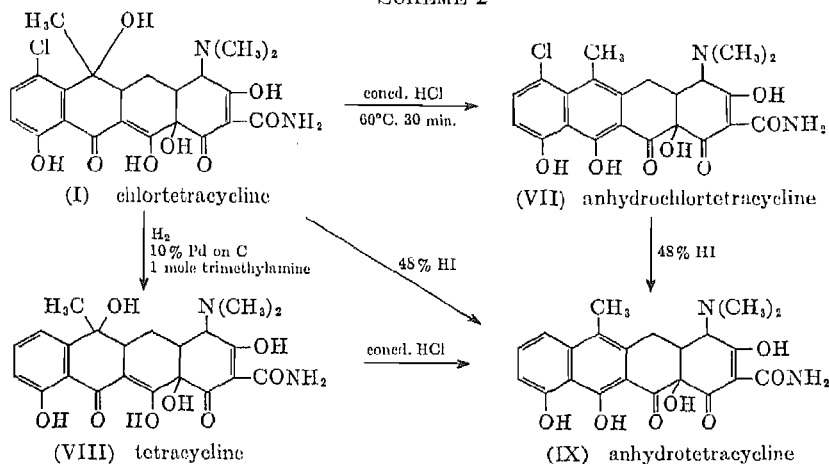


(11,12,25-28). The formation of **isochlortetracycline** (II) involves the alkaline cleavage of a C—C bond of an enolizable  $\beta$ -diketone to form a carboxyl group that subsequently lactonizes to give a phthalide. The reaction leading to the formation of  **$\alpha$ -aureomycinic acid** (III) from isochlortetracycline involves a ketonic hydrolysis and the production of a carboxyl group from the nonconjugated  $\beta$ -diketone of isochlortetracycline (11,12,25-28).

In a series of degradation reactions with acid similar to that of oxytetracycline (see p. 794), chlortetracycline yields **desdimethylaminochlortetracycline** after 6 hours of treatment with zinc and acetic acid. On prolonged treatment with these reagents chlortetracycline gives **desdimethylamino-12a-deoxychlortetracycline**. When treated with hydrochloric acid in methanol, desdimethylaminochlortetracycline yields **desdimethylaminoanhydrochlortetracycline**, which is similar in structure to anhydrochlortetracycline (VII), while desdimethylamino-12a-deoxychlortetracycline gives **desdimethylamino-6,12a-dideoxychlortetracycline**, which on distillation with zinc dust yields the basic skeleton of the tetracyclines, naphthacene. If desdimethylamino-12a-deoxychlortetracycline is treated with alkali, **desdimethylamino-**



SCHEME 2



**12a-deoxyisochlortetracycline**, similar in structure to isochlortetracycline (II), is obtained.

Scheme 2 summarizes some of the reactions with acid and the reduction of chlortetracycline (3,6,28).

Of the many degradation products made available by the structure studies, only those shown in Scheme 2 have been reported to have more than very slight antibacterial action. Tetracycline has antibiotic activity very similar to that of chlortetracycline (3,6) (see p. 805). The anhydro compounds (for example, anhydrochlortetracycline) have some biological action, but less than those of the parent compounds (24). Apparently for antibiotic action the tetracyclic hydroaromatic ring system as a whole must be retained. The presence or orientation of individual peripheral groups or individual specific ring systems by themselves are not responsible for full potency.

See also references 13,15,20.

### Preparation and Manufacture

**Organism Producing Antibiotic.** Chlortetracycline is prepared from the culture broth of *Streptomyces aureofaciens*, the cultural characteristics and certain biochemical properties of which have been described in some detail by Duggar (7,34). Extreme variability in microscopic, macroscopic, and physiological characteristics occurs in natural, spontaneous, and in artificially induced mutant strains of this species (2). Van Dyck and De Somer (23) attempted to correlate mycelium pigmentation and chlortetracycline production of their mutant strains obtained by ultraviolet light irradiation. The most stable cultures and best producers were found to be yellow in color.

Katagiri (14) also investigated the correlation of morphology with chlortetracycline production. He divided the colonies of his strain W227-H-13, grown on a modified Van der Brook sporulation medium, into three types (by form of colony and color of conidia produced) and found that there was no apparent difference in antibiotic production between the three colony types. However, when grown on glucose nutrient agar, there was a close correlation of morphological properties with chlortetracycline production capacity, in that heavily spored colonies gave lower po-

tendencies than normal nonspored colonies, and colonies with strong pigmentation were more potent than those with a pale or hyaline mycelium.

*Maintenance of Culture.* Van Dyck and De Somer (23) and Katagiri (14) reported that, in the absence of special precautions, degeneration took place in their selected strains. The former authors stated that spores preserved in a lyophilized form showed good preservation for some months, and the latter author found that strains retained their high state of antibiotic production when spores were stored in sterile, desiccated soil in an ice box for 2 months.

As with streptomycin (see p. 70), an actinophage also has been isolated from cultures and fermentor broths of *Streptomyces aureofaciens*. Weindling and Kapros (29) obtained phage-resistant strains from such infected material; some of the resistant strains were lysogenic, while others were not.

**Fermentation Procedure.** Chlortetracycline is produced commercially by submerged culture in deep tanks with aeration and constant agitation of the broth. Carbon steel, stainless steel, and glass-lined tanks of various sizes can be used. The medium is sterilized with steam and the fermentation is conducted under sterile conditions. Both natural and synthetic media have been developed for the chlortetracycline fermentation (see Table I). Besides sucrose, other sources of energy or carbon that may be used are starch, dextrin, maltose, dextrose, lactose, mannitol, and glycerol. Suitable sources of nitrogen include a wide variety of substances such as amino acids, peptones, casein, corn steep liquor, meat extracts, molasses, fish solubles, various oil-extracted seed meals, as well as chemicals such as urea, nitrates, and ammonium compounds. In common with most fermentation processes, the medium should also contain certain inorganic elements such as phosphorus, potassium, calcium, magnesium, chlorine, sulfur, and what are commonly known as trace elements. Under many conditions sufficient of all of these elements are present as impurities or are contained in such crude nutrient substances as the corn steep liquor, molasses, etc., so that additional quantities of the salts need not be added to the medium.

The vegetative or *preformed inoculum* originates from the growth of mycelium and spores on the surface of an agar slant. This is used to inoculate media in shaker flasks. The flasks are then used to inoculate media in aerated bottles. These bottles are employed as inoculum for small tanks known as seed tanks, 1-5% of this fermenting medium is the inoculum for the large production tanks. The media of the various inoculum stages may or may not be the same as that for the main tank, and growth takes place at 26-28°C. for about one or two days. The fermentations in the final production tanks proceed at 27°C. for 24-72 hr. or longer, depending upon the medium and the amount of inoculum used. Continuous agitation and aeration of the medium can be carried out with various types of agitators and aerators. A rate of aeration of about 0.2-3.0 liters of air per liter of medium per minute can be used, but the actual aeration may vary and will depend upon the kind of agitator used and the rate at which it is operated, the type of aerator (open-end, nozzle, sparger, etc.), and other tank conditions. Excessive foaming of the medium may be controlled by the aseptic addition of a sterile antifoam agent such as lard oil. Foaming is also reduced, as is the danger of contamination, by operating the tanks with a positive internal pressure of 1-10 p.s.i.g.

For maximum growth and antibiotic production it is necessary that the pH of the fermentation medium be controlled within rather narrow limits, approximately 6-7. For this purpose 0.25-1% of calcium, barium, or strontium carbonate has been found

to be particularly useful, as well as 0.25–1.5% magnesium phosphate. Because the antibiotic is a sparingly soluble weak base, some of it may be precipitated as the metal-

TABLE I. Fermentation Media and Approximate Yields.

A. Natural Type		
Duggar (34)	Niedercorn (37)	Van Dyck and De Somer (23)
1% sucrose	3% sucrose	2.75% sucrose
1% corn steep liquor	2% corn steep liquor	1.75% peanut oil meal
0.2% $(\text{NH}_4)_2\text{HPO}_4$	0.625% $\text{CaCO}_3$	0.5% $\text{CaCO}_3$
0.2% $\text{KH}_2\text{PO}_4$	0.2% $(\text{NH}_4)_2\text{SO}_4$	0.3% $\text{NaCl}$
0.1% $\text{CaCO}_3$	0.005% $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$	0.25% $(\text{NH}_4)_2\text{SO}_4$
0.025% $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$	0.00033% $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$	0.25% corn steep liquor
0.005% $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$	0.00033% $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$	0.15% molasses
0.00033% $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$	396 $\gamma/\text{ml}$ .	Initial pH 6.5
0.00033% $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$		1,250 $\gamma/\text{ml}$ .
Initial pH 6.3		
170 $\gamma/\text{ml}$ .		
Petty (33)	Katagiri (14)	
3% sucrose	3.5% soybean oil meal	5% starch
3% corn steep liquor	2.5% starch	0.35% $\text{CaCO}_3$
0.9% $\text{CaCO}_3$	0.5% dried yeast	0.3% peptone
0.33% $(\text{NH}_4)_2\text{SO}_4$	0.35% $\text{CaCO}_3$	0.25% $(\text{NH}_4)_2\text{SO}_4$
0.2% $\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$	0.25% $\text{NaCl}$	0.1% $\text{K}_2\text{HPO}_4$
0.1% $\text{NH}_4\text{Cl}$	0.005% $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$	0.1% $\text{KCl}$
0.01% $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$	0.0005% $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$	0.05% meat extract
0.005% $\text{MnSO}_4 \cdot 4\text{H}_2\text{O}$	0.0005% $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$	0.025% $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$
0.0041% $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$	KOH to pH 7.2	KOH to pH 7.2
0.0005% $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$	1,560 $\gamma/\text{ml}$ .	450 $\gamma/\text{ml}$ .
pH 6.4 after sterilization.		
0.3% lard oil added		
as antifoam agent.		
2,500 $\gamma/\text{ml}$ .		
B. Semisynthetic and Synthetic Types		
Niedercorn (37)	Petty, Goodman, and Matrishin (10)	
3% sucrose	3% sucrose	
1% casein	Glycine <sup>a</sup>	
0.25% $\text{CaCO}_3$	0.75% $\text{Mg}$ lactate	
0.18% ammonia	0.5% $\text{CaCO}_3$	
0.166% $(\text{NH}_4)_2\text{SO}_4$	0.2% $\text{K}$ lactate	
0.05% $\text{KCl}$	0.2% $(\text{NH}_4)_2\text{HPO}_4$	
0.05% $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$	0.2% $(\text{NH}_4)_2\text{SO}_4$	
0.005% $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$	0.1% $\text{KCl}$	
0.001% $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$	Traces of $\text{Fe}$ , $\text{Mn}$ , $\text{Zn}$ , $\text{Cu}$ , $\text{Co}$	
0.0004% $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$	650 $\gamma/\text{ml}$ .	
0.00033% $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$		
0.00033% $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$		
Initial pH 7.7		
245 $\gamma/\text{ml}$ .		
	<sup>a</sup> Quantity not stated; it serves as N source in the final fermentation medium, but the inoculum is grown in the above salt formula with a combination of alanine, arginine, methionine, glutamic acid, histidine, and asparagine as the organic N source.	

lic salt by the above bivalent cations. Details of the entire chlortetracycline fermentation are outlined in the various references given in Table I. The actual yields of antibiotic are dependent upon the medium, the process, and the strain of organism that is used.

**Isolation and Purification.** Various processes relying upon the physical and chemical properties of chlortetracycline have been devised for recovering it from the fermentation liquors.

Pidaeks and Starbird described a chromatographic adsorption method (35). The clear, fermented broth filtrate (pH 4.65) was adsorbed on magnesium silicate (Florisol). The column was washed with water and then with a small amount of acetone to remove colored impurities. Acid methanol (pH < 5) was used to develop the column into three distinct bands when observed by ultraviolet light: a blue band containing little activity, a yellow band containing the bulk of the antibiotic, and a dull brown band containing about 5% of the activity. The eluate of the yellow band was concentrated to dryness *in vacuo*, and the dry product extracted with *n*-butyl alcohol. The butyl alcohol extract was washed with water and then concentrated *in vacuo* to a small volume. Acetone was added to this concentrate to precipitate impurities, which were filtered off. Absolute ether was then added to the filtrate to precipitate the antibiotic.

Van Dyck and De Somer (23) used a solvent-carrier method of isolation. Oxalic acid and ammonium oxalate were added to the fermented broth to pH 3.6. The solids were removed by filtration. The clear filtrate was extracted with an organic solvent (amyl alcohol, methyl isobutyl ketone, or *n*-amyl acetate) containing 3–5% of a surface-active agent (for example, lauric acid at pH 8). The organic solvent phase was removed, acidified to pH 1.7 with 20% sulfuric acid, and allowed to stand for spontaneous crystallization of the chlortetracycline. These authors also found that the maximum adsorption of this antibiotic on synthetic resins of the carboxyl type took place between pH 3.5 and 4. However, they were unable to report an effective elution procedure, so this method could not be used for purification.

Harms (39) and Starbird and Pidaeks (30) have described methods for the recovery of chlortetracycline from fermentation broths. The antibiotic is separated as an insoluble salt of a bivalent metal (Ca, Ba, Mg, Sr) together with the mycelium and other solids of the broths at a pH of about 8.5. The antibiotic is subsequently extracted from these separated solids with wet acetone at pH 1.5 or 10. The antibiotic in the alkaline cake or in the original fermentation broth could also be obtained in aqueous solution by adjusting the pH to about 1.5, mixing, and filtering off the insoluble solids. An aqueous concentrate of chlortetracycline was obtained by distilling off the acetone or water *in vacuo*. Crystals were isolated from this concentrate after adding 25–30% sodium chloride and 5% *n*-butyl alcohol, mixing, and chilling.

An acid-butyl alcohol separation process is described by Hallock and Muller (31). The chlortetracycline in the fermentation broth is precipitated as an insoluble salt of a bivalent metal and is separated, together with the mycelium and filter aid (2%), such as magnesium silicate and diatomaceous earth. The filtrate is discarded and the separated solids are extracted with drying, using *n*-butyl alcohol at pH 0.5–2.5. The *n*-butyl alcohol extract is treated with about 0.25% of activated carbon (for example, Darco G-60). After the charcoal is removed, the clarified extract is concentrated *in vacuo* to a crystal slurry. This concentrate is chilled in the presence of acid and 2-ethoxyethanol (Cellosolve). The crystals are separated, washed successively with Cellosolve, water, and anhydrous ethyl alcohol, and dried.

Winterbottom *et al.* (32) reported a method for the separation of chlortetracycline from aqueous acid (pH 2) solution that involves its interaction with an anionic organic sulfuric acid derivative ( $\text{ROSO}_3\text{H}$ ) to form a salt-type compound. The latter may be separated by extraction into methyl isobutyl ketone and recovered as such, or it can be resolved into the hydrochloride salt of the antibiotic in the presence of hydrochloric acid (pH 1) and excess ammonium chloride and crystallized from Cellosolve.

Winterbottom *et al.* (40) also described a method for the purification of chlortetracycline whereby the amorphous form is converted to a comparatively pure crystalline form, and the purity and yield of crystalline preparations can be improved. In general, the antibiotic is suspended in a solvent such as cold Cellosolve and caused to dissolve by adding triethylamine to about pH 8 (2 equivalents). Impurities insoluble in this alkaline solution are filtered off, and colored impurities are removed by adsorption on activated charcoal. The chlortetracycline may be recovered in the desired form from the alkaline solution by altering the characteristics of the system. To obtain an acid salt, enough of the desired acid is added to shift the pH to less than 3 (for example, hydrochloric acid to pH 0.8). To obtain the neutral antibiotic, the pH is adjusted to about 6. To obtain an alkali metal salt, such as the sodium or potassium salt, the pH is adjusted to about 8–10, and methanol is added to make the salt less soluble. Crystals of the various forms are first washed with the solvent from which they were originally recovered, then with a small amount of water, next with ethyl alcohol, and then they are dried for use.

**Market Forms.** Chlortetracycline is marketed in a number of forms and strengths for human and veterinary therapy (110) and their use depends upon the method of administration desired and the clinical circumstances of the patient.

Capsules of chlortetracycline hydrochloride with filler substance are marketed for oral use, as are drops and a sirup containing chlortetracycline calcium equivalent to 100 mg./cc. and 125 mg./4 cc. of the hydrochloride, respectively, and a chocolate-flavored powder to be dissolved in warm milk or water. Chlortetracycline hydrochloride in crystalline form, buffered with sodium glycinate is available in sterile vials for intravenous administration.

Topical preparations containing chlortetracycline hydrochloride include surgical and vaginal powders, vaginal and rectal suppositories, an ointment for minor cuts or abrasions, and various ophthalmic, otic, and oropharyngeal forms. Other preparations available for specific purposes are dental cones, ointment, and paste and impregnated surgical dressings.

For veterinary use oral drops and capsules and intravenous preparations similar to the forms for human therapy are available, as well as ointments, soluble powders for addition to the drinking water of poultry and livestock, and a therapeutic food supplement with added vitamin  $\text{B}_{12}$ . Nutritional animal feed preparations containing chlortetracycline hydrochloride (the residue of the manufacture of the crystalline antibiotic) and vitamin  $\text{B}_{12}$  are on the market. The antibiotic used in these nutritional preparations is assayed to guarantee the amount of the drug in each mixture.

**Stability.** In the dry state, the antibiotic is stable indefinitely, and neither the base nor the hydrochloride is affected appreciably by moisture. The hydrochloride can be sterilized by dry heat at 110–120°C. for 10–15 hours without loss of potency. The crystalline alkaline salts, for example, the sodium salt, are also stable in the dry state but are much more sensitive to high moisture levels. All the salts show some degree of sensitivity when exposed to strong, direct sunlight. This phenomenon is characterized by surface darkening without detectable loss of potency.

The stability of chlortetracycline in aqueous solutions is strictly a function of pH, optimum stability being attained below pH 3.0. Thus, a solution of the hydrochloride (pH 2.5–2.8) has a half-life of 14 days at room temperature and can be maintained for several months at 4°C. without appreciable loss of potency. At pH 8.5 the antibiotic shows a half-life of 4 hours. Suspensions of the base in water are stable indefinitely.

### Microbiological Properties

**Antimicrobial Activity.** Chlortetracycline is active *in vitro* against numerous Gram-positive and Gram-negative organisms (51,53,95,107,109,112,132). These include *Diplococcus pneumoniae*, *Neisseria* strains, streptococci, staphylococci, *Escherichia*, *Brucella*, *Bacillus cereus* and *B. subtilis*, *Klebsiella pneumoniae*, *Aerobacter aerogenes*, *Hemophilus influenzae*, *H. ducreyi*, *Pasteurella* strains, and *Clostridium* strains. The effectiveness of chlortetracycline against pathogenic rickettsiae and large viruses of the psittacosis and lymphogranuloma venereum group has been shown in experimentally infected animals and man (41,88,118,125,143). Of the fungi, *Actinomyces* has been found sensitive (103) and, of the protozoa, *Endamoeba histolytica*, by *in vitro* test and clinical trial (83,101). *Treponema pallidum* and *T. pertenue* are sensitive as determined by clinical response (97,141). Although *in vitro* studies indicated that *Mycobacterium tuberculosis* was inhibited by chlortetracycline, subsequent clinical trial has shown it to be ineffective clinically (134). Chlortetracycline, although effective in experimental malaria, is not practical for use in man owing to the high dosages necessary to produce a therapeutic effect (59a) (see also Vol. 8, p. 677). Nearly all strains of *Proteus vulgaris* and *Pseudomonas aeruginosa* are resistant (107), although an occasional strain may be quite sensitive (124).

*In vitro* sensitivity tests are influenced by such factors as the number of organisms in the inoculum, their phase of growth, and the pH of the test medium. The most reliable method for determination of *in vitro* sensitivity is the method of Dornbush and Pelcak (66). Since chlortetracycline deteriorates rapidly in culture media at incubator temperatures, *in vitro* test systems should be read within 4–24 hours; 48- to 72-hour tests are of dubious value.

The antibiotic is primarily bacteriostatic in action, but in higher concentrations it does have a bactericidal effect. Its specific mode of action is not known, but it is thought that it interferes with some enzyme system necessary for the growth and reproduction of the infectious agent (see p. 773; see also ref. 124a).

**Development of Resistance.** Tolerance to chlortetracycline may be induced by the serial subculture technique fairly readily in most strains of Gram-negative bacilli; less readily in some strains of staphylococci; and with considerable difficulty in streptococci, especially of the  $\beta$ -hemolytic type (106). Resistance is rarely increased more than two-, four-, or eightfold, and the acquired resistance tends to disappear promptly after exposure to the antibiotic has ceased (95). Organisms have not been observed to produce a substance antagonistic to chlortetracycline comparable to penicillinase (see Vol. 9, p. 926), and no chlortetracycline-dependent organisms have been encountered (94).

The development of resistance to the antibiotic has not been a clinical problem (47,81,94). The conditions required for inducing resistance *in vitro* do not obtain when chlortetracycline is used therapeutically. In the *in vitro* technique, the organisms are first grown in the presence of subinhibitory concentrations of chlortetracycline and the

concentrations are gradually increased; whereas, clinically, inhibitory levels are immediately attained and are maintained continuously.

In a variety of infections caused by Gram-positive and Gram-negative organisms (including staphylococci, streptococci, paracolon bacilli, and *Spirillum minus*), the causative organism was isolated and tested in several cases both before chlortetracycline therapy and after a period of treatment. No resistance to chlortetracycline developed in any organisms in cases in which prolonged administration was necessary (93). Clinical studies revealed no evidence of the development of resistance by amebas (*Endamoeba histolytica*) to chlortetracycline (102). Other reports have referred to the failure to encounter the development of resistance by staphylococci in puerperal mastitis (89) and osteomyelitis (52).

That resistance to chlortetracycline is acquired by a microorganism during the course of therapy is generally difficult to prove, since the possibility always exists that "superinfection" with a naturally resistant strain might have occurred (65,70,106).

### Pharmacological Properties

**Absorption and Excretion.** When given orally, chlortetracycline readily passes into the blood stream, maintaining measurable serum levels for as long as 12 hours (68), and thence passes into the spinal fluid, peritoneal fluid (117), pleural fluid, bile, urine, and milk (82,90), diffusing widely throughout all the body tissues. The presence or absence of inflammation is not a factor controlling diffusion through the blood-brain barrier (82). The antibiotic has been found in the liver, kidney, lung, and spleen and can diffuse through the placenta to enter the fetal circulation (82). Doses of 5–10 mg./kg. of chlortetracycline, given orally at 6-hour intervals, insure the persistence of measurable blood levels (90). After 700 mg. of chlortetracycline was given orally to adults, the peak concentration in the serum occurred at about the sixth hour, and all sera showed detectable amounts at the twelfth hour. The highest blood levels occurred 2 hours after oral administration of 300 mg. (2  $\gamma$ /ml.) (143).

In dogs given 3 intravenous doses of 20 mg./kg. at 2-hour intervals, the chlortetracycline readily passed the blood-brain barrier, and substantial amounts remained in the blood stream (40  $\gamma$ /ml.), and in the cerebrospinal fluid (0.8  $\gamma$ /ml.) 2 hours after the last injection (114). When doses of 0.05 g. are given intravenously to humans, the serum concentration rises sharply to between 0.6 and 5.0  $\gamma$ /ml. within 5 minutes and then declines gradually during the next 6 hours (48). Very high levels are found in the bile and significant amounts in the intestines after intravenous administration. Intramuscular injection of 20 mg./kg in rabbits and 40 mg./kg. in dogs gave levels of 0.3–1.25  $\gamma$ /ml. from 15 to 60 minutes after injection, but significant levels did not persist after 1 hour. After intramuscular injection of 100 mg. in adult humans, the peak concentration in the blood was reached at about the third hour (68). There is little or no absorption into the blood stream when chlortetracycline is given as a retention enema (85).

After oral administration of chlortetracycline hydrochloride to rats, the rate of excretion remained relatively constant for at least 6 hours, and in man the drug is excreted in high concentration in the urine (90) and can be detected for as long as 55 hours after a single oral dose of 0.5 or 0.75 g. (107). After intravenous injection in dogs, the excretion was rapid during the first 2 hours, slower between the second and fourth hours, and low between the fourth and sixth hours.

**Toxicity.** The toxicity of chlortetracycline is relatively low (80,126). The drug shows a mortality rate in mice of 5% at an oral dosage of 2,500 mg./kg. Animals given chlortetracycline orally for as long as 15 weeks were found to have suffered no ill effects. The approximate LD<sub>50</sub> for intravenous administration in mice is between 50 and 100 mg./kg. (50). No health impairment was observed 1 month after a series of intravenous doses had been given to dogs. Unanesthetized dogs given 3 doses intravenously of 20 mg./kg. each and 2 doses orally of 50 mg./kg. each in 24 hours showed no toxic symptoms. Little or no subacute toxicity was observed after administration of chlortetracycline. Low toxicity was also observed after multiple intramuscular injections, except that these doses were locally irritating. Furthermore, no chronic toxicity appeared to result. The LD<sub>50</sub> for subcutaneous injection was between 3,000 and 4,000 mg./kg.

Daily oral administration of 15–30 mg./kg. of chlortetracycline in both patients and normal individuals showed no toxicity (50). No evidence of renal impairment, jaundice, or change in icteric index, cephalin flocculation, or prothrombin was found. Repeated blood examinations did not indicate any anemia, hemolysis, leukopenia, or thrombopenia. Blood-chemistry tests showed normal values for total protein, albumin-globulin content or ratio, cholesterol, carbon dioxide, and alkaline phosphatase values. In the oral treatment with chlortetracycline of about 100 patients experiencing a variety of bacterial infections, significant toxic effects other than minor side effects were notably absent, although the dosage was large (59).

The antibiotic in use today is one of extremely high purity and is comparatively free of the gastrointestinal side reactions characteristic of the earlier drug (43,77). The diarrhea which sometimes occurs after several days of oral therapy with chlortetracycline is probably a result of marked inhibition of the intestinal flora and not a toxic reaction. Other side effects are the burning of the tongue and pruritis. After prolonged therapy, particularly in debilitated patients, monilial overgrowth has been reported, which is probably due to changes in the normal flora brought about by the profound antibacterial action of the antibiotic (64,128). Allergic reactions in the form of urticaria, rash, and fever will occur, but the incidence is extremely low (67).

The intravenous administration of chlortetracycline in dogs and cats appeared to be free of antipyretic action and to have no significant effect on blood pressure or on the response to histamine, epinephrine, acetylcholine, or faradic stimulation of the vagus. No electrocardiographic changes were caused by doses up to 50 mg./kg., and only minor and temporary effects by doses between 50 and 100 mg./kg. No significant effects were observed upon respiration or urinary activity. Chlortetracycline was essentially without effect on the blood sugar, or on the activity of the isolated gut or uterus of the guinea pig. Chlortetracycline seemed also to have no effect on the central nervous system, and no evidence of methemoglobin formation was detected after intravenous dosage.

With intravenous administration, excessive dosage may sometimes cause jaundice and abnormal liver function tests which are reversible by cessation of therapy (91). Phlebitis at the site of injection may also be encountered during intravenous administration. In a report (143) on the treatment of 35 cases of lymphogranuloma venereum by chlortetracycline, it was found that the antibiotic was non-toxic.

**Administration and Dosage.** The systemic administration of chlortetracycline may be carried out by utilizing either the oral or the intravenous form; the intravenous



form is intended for use in patients who are unable to take the antibiotic orally. The intramuscular route is not feasible because of considerable irritation and pain at the site of injection. The average oral dose for adults and children is 12.5–20 mg./kg. of body weight per day and is given in divided doses every 6 hours. Increasing the oral dose of chlortetracycline beyond 1.0 g. daily does not proportionately increase blood concentrations. Divided doses of 0.25 g. every 6 hours have given levels almost as satisfactory as those following doses of 0.5, 0.75, or 1.0 g. every 6 hours (48). The adult intravenous dose is 500 mg. every 12 hours, with proportionately less for children.

For veterinary use, chlortetracycline should be given only by intravenous injection in bovines and equines, except in young calves that are not yet ruminating. These calves may be given the drug orally.

### Specifications and Assay

**Specifications.** Chlortetracycline and its preparations became certifiable drugs under an amendment to the Food, Drug, and Cosmetic Act in 1949. Under the law each batch is examined by the Food and Drug Administration and certified prior to shipment in interstate commerce. The complete procedures may be found in the Federal Registry (73); the identification, solubility, specific rotation, pH of solution, loss on drying, heavy metals, safety (toxicity), and potency (not less than 97% by the fluorometric assay (73)) must be established.

Parenteral-grade preparations are tested for presence of pyrogens and blood-depressor substances and for sterility.

**Assay.** The potency of chlortetracycline preparations may be determined by either physicochemical or microbiological methods (66,73,84,92). The physicochemical methods as a group are limited to the high-potency, relatively pure preparations, although the fluorometric method can be used for routine assays when it is known that certain impurities similar in chemical nature to the antibiotic are not present.

The antibiotic activity of chlortetracycline is rapidly lost in alkaline solutions, and with progressive alkaline degradation there is a concomitant increasing fluorescence. This is the basis of the *fluorometric method*, and the pH of the solution determines the rate at which fluorescence develops. In very weak alkaline solutions the rate of development of fluorescence is slow enough to be measured and intensifies with increasing temperature.

The *colorimetric method* depends upon the stable yellow color which develops when chlortetracycline is treated with a strong acid. The absorbance curve obtained shows a characteristic wave length. The change in absorbance is due to the acid treatment and is proportional to the concentration of the chlortetracycline.

The microbiological method is readily applied to the assay of crude preparations such as fermentation broths and the antibiotic feed supplements, as well as to other preparations (73). Turbidimetric and agar diffusion procedures are used in microbiological assays (66). The most common turbidimetric method uses *Micrococcus pyogenes* var. *aureus* as the test organism, and one of the agar diffusion methods uses *Sarcina lutea*.

### Uses and Indications

**Human Medicine.** A very wide variety of infections will respond to the action of this antibiotic, testifying to the broad-spectrum nature of its antimicrobial action

(49,51,59,61,86,88,101,104,105,111,116,123-126,132,133,142,143). The following conditions are indications for chlortetracycline therapy: Gram-positive infections, including those caused by streptococci, staphylococci, and pneumococci; Gram-negative infections, including those caused by some of the coli-aerogenes group; bacterial infections associated with virus influenza; bacterial and virus-like infection of the eye; *Bacteroides* septicemia; brucellosis; chancreoid; Friedländer infections; gonorrhea; peritonitis; pertussis infections; leptospiral infections; sinusitis; endocarditis; trachoma; tularemia; typhus; the common infections of the uterus and adnexa; viral infections such as granuloma inguinale, *Hemophilus influenzae* infections, primary atypical pneumonia, psittacosis, and lymphogranuloma venereum; Q fever and other rickettsial infections; yaws; acute intestinal amebiasis; and as an adjunct to surgery in a wide variety of surgical infections.

In regard to syphilis, chlortetracycline is second only to penicillin and is used in patients in which penicillin is contraindicated (54,115).

Chlortetracycline has been used locally and systemically with favorable results in treating a variety of dental conditions (56,71,72,74,75,119,120). These include localized osteitis or dry socket, acute alveolar abscessa, cellulitis, phlegmon, Ludwig's angina, osteomyelitis, herpetic gingivostomatitis, and Vincent's infection.

**Veterinary Medicine.** Chlortetracycline is indicated in a wide variety of animal diseases (42,45,55,63,69,76,79,98,130,135,138): bovine infections such as calf scours and pneumonia, foot rot, anaplasmosis, chronic bloat, vibriosis, and early treatment of "black leg"; equine infections, including strangles, septicemias, infected wounds, and shipping fever; and swine infections, including the enterites such as dysentery, salmonellosis, baby pig diarrhea, and pneumonia. Since special periods of stress such as vaccination, extreme temperatures, and moving or other changes in management may reduce resistance to the above diseases, the use of this antibiotic is indicated during such periods. Small-animal conditions such as pneumonia, sinusitis, and tonsillitis respond to chlortetracycline, as do gastrointestinal infections, bacterial infections associated with distemper, leptospirosis, coccidiosis, local infections, cystitis, nephritis, feline infectious enteritis, and feline coryza. Chlortetracycline is indicated in poultry farming for stimulation of feed intake, maintenance of weight gains, reduction of mortality in the presence of chronic respiratory disease, blue comb of chickens, and also in periods of stress.

**Nutrition Supplements.** In connection with work on the "animal protein factor" (78,100,113,121,122,136) (see Vol. 6, p. 311), it was found that crude chlortetracycline fermentation mash (containing some vitamin B<sub>12</sub> (see *Vitamins*)) gave growth responses in animals well above those obtained with supra-optimal levels of vitamin B<sub>12</sub> (44,60,62,87,96,99,129). At the present time, animal feeds containing supplements of chlortetracycline mixtures are being used extensively for growth stimulation and improvement of feed efficiency, and for the reduction of losses from certain disease conditions. The action of antibiotics in increasing growth apparently is confined to their effect on the bacteria within the intestinal tract (57).

Following the observations on increased growth rate in animals, a possible similar effect was looked for in humans. Studies on premature infants (108,114,131) indicated that growth rate is increased and morbidity is lessened. A large-scale study in poorly developed and undernourished children was carried out, and children receiving 50 mg. of chlortetracycline per day increased in weight and height over their controls during an 18-month period (127).

Another possible use of chlortetracycline is its application in the preservation of foods. To date it has been tried in preserving beef, pork, lamb, fish, and poultry with encouraging results (137,139). Chlortetracycline may also be useful in the field of plant pathology.

### Bibliography

- (1) Albert, A., *Nature*, **172**, 201 (1953).
- (2) Backus, E. J., Duggar, B. M., and Campbell, T. H., *Ann. N.Y. Acad. Sci.*, in press.
- (3) Boothe, J. H., Morton, J., II, Petisi, J. P., Wilkinson, R. G., and Williams, J. H., *J. Am. Chem. Soc.*, **75**, 4621 (1953).
- (4) Brochard, R. W., Dornbush, A. C., Gordon, S., Hutchings, B. L., Kohler, A. R., Krupka, G., Kushner, S., Lefemine, D. V., and Pidacks, C., *Science*, **109**, 199 (1949).
- (5) *C.A.*, **46**, 13363 (1952).
- (6) Conover, L. H., Moreland, W. T., English, A. R., Stephens, C. R., and Pilgrim, F. J., *J. Am. Chem. Soc.*, **75**, 4622 (1953).
- (7) Duggar, B. M., *Ann. N.Y. Acad. Sci.*, **51**, 177 (1948).
- (8) Dunitz, J. D., and Leonard, J. E., *J. Am. Chem. Soc.*, **72**, 4276 (1950).
- (9) Dunitz, J. D., and Robertson, J. H., *J. Am. Chem. Soc.*, **74**, 1108 (1952).
- (10) Hiscox, D. J., *J. Am. Pharm. Assoc.*, **40**, 237 (1951).
- (11) Hutchings, B. L., Waller, C. W., Gordon, S., Brochard, R. W., Wolf, C. F., Goldman, A. A., and Williams, J. H., *J. Am. Chem. Soc.*, **74**, 3710 (1952).
- (12) Hutchings, B. L., Waller, C. W., Brochard, R. W., Wolf, C. F., Fryth, P. W., and Williams, J. H., *J. Am. Chem. Soc.*, **74**, 4980 (1952).
- (13) Johnson, A. W., *Science Progr.*, **41**, 473 (1953).
- (14) Katagiri, K., *J. Antibiotics Japan*, **A7**, 45 (1954).
- (15) Kuhn, R., and Dury, K., *Chem. Ber.*, **84**, 563 (1951).
- (16) Levine, J., Garlock, E. A., Jr., and Fischbach, H., *J. Am. Pharm. Assoc.*, **38**, 473 (1949).
- (17) Parke, T. V., and Davis, W. W., *Anal. Chem.*, **26**, 642 (1954).
- (18) Pepinsky, R., and Watanabe, T., *Science*, **115**, 541 (1952).
- (19) Petty, M. A., Goodman, J. J., and Matrishin, M., Summary of Papers, VIth International Congress of Microbiology, Rome, Italy, Sept. 1953, Vol. I, p. 156.
- (20) Regna, P. P., *Trans. N.Y. Acad. Sci.*, **15**, No. 1, 12 (1952).
- (21) Stephens, C. R., Conover, L. H., Hochstein, F. A., Regna, P. P., Pilgrim, F. J., Brunings, K. J., and Woodward, R. B., *J. Am. Chem. Soc.*, **74**, 4976 (1952).
- (22) Stephens, C. R., Conover, L. H., Pasternack, R., Hochstein, F. A., Moreland, W. T., Regna, P. P., Pilgrim, F. J., Brunings, K. J., and Woodward, R. B., *J. Am. Chem. Soc.*, **76**, 3568 (1954).
- (23) Van Dyck, P., and De Somer, P., *Antibiotics & Chemotherapy*, **2**, 184 (1952).
- (24) Waller, C. W., Gordon Research Conference, New London, N.H., Aug. 20, 1952.
- (25) Waller, C. W., Hutchings, B. L., Wolf, C. F., Brochard, R. W., Goldman, A. A., and Williams, J. H., *J. Am. Chem. Soc.*, **74**, 4978 (1952).
- (26) Waller, C. W., Hutchings, B. L., Goldman, A. A., Wolf, C. F., Brochard, R. W., and Williams, J. H., *J. Am. Chem. Soc.*, **74**, 4979 (1952).
- (27) Waller, C. W., Hutchings, B. L., Wolf, C. F., Goldman, A. A., Brochard, R. W., and Williams, J. H., *J. Am. Chem. Soc.*, **74**, 4981 (1952).
- (28) Waller, C. W., Hutchings, B. L., Brochard, R. W., Goldman, A. A., Stein, W. J., Wolf, C. F., and Williams, J. H., *J. Am. Chem. Soc.*, **74**, 4981 (1952).
- (29) Weindling, R., and Kapros, C., *Bacteriol. Proc.*, **1951**, 48.
- (30) Can. Pat. 497,340 (Nov. 3, 1953), E. E. Starbird and C. Pidacks (to American Cyanamid Co.).
- (31) Can. Pat. 497,343 (Nov. 3, 1953), W. K. Hallock and S. A. Muller (to American Cyanamid Co.).
- (32) Can. Pat. 497,344 (Nov. 3, 1953), R. Winterbottom, H. Mendelsohn, S. A. Muller, and J. R. D. McCormick (to American Cyanamid Co.).
- (33) Can. Pat. 499,648 (Feb. 2, 1954), M. A. Petty, Jr. (to American Cyanamid Co.).
- (34) U.S. Pat. 2,482,055 (Sept. 13, 1949), B. M. Duggar (to American Cyanamid Co.).
- (35) U.S. Pat. 2,586,766 (Feb. 19, 1952), C. Pidacks and E. E. Starbird (to American Cyanamid Co.).
- (36) U.S. Pat. 2,603,584 (July 15, 1952), C. Pidacks and G. M. Sieger (to American Cyanamid Co.).
- (37) U.S. Pat. 2,600,329 (Sept. 2, 1952), J. G. Niedercorn (to American Cyanamid Co.).

- (38) U.S. Pat. 2,640,842 (June 2, 1953), J. F. Weidenheimer, C. C. Reed, L. Ritter, and S. D. Upham (to American Cyanamid Co.).
- (39) U.S. Pat. 2,658,077 (Nov. 3, 1953), E. R. Harms (to American Cyanamid Co.).
- (40) U.S. Pat. 2,671,806 (Mar. 9, 1954), R. Winterbottom, P. Eichler, and C. Pidaeks (to American Cyanamid Co.).
- (41) Anigstein, L., Whitney, D., and Beninson, J., *Ann. N.Y. Acad. Sci.*, **51**, 306 (1948).
- (42) Archibald, J., and Choppel, C. I., *Can. J. Comp. Med. Vet. Sci.*, **14**, 190 (1950).
- (43) Bartholomew, L. G., and Nichols, C. R., *Proc. Staff Meetings Mayo Clinic*, **25**, 370 (1950).
- (44) Bartley, E. E., Fountaine, F. C., and Atkeson, F. W., *J. Animal Sci.*, **9**, 646 (1950).
- (45) Bartree, A. L., Shook, J. C., Chang, K. H., and Dowdy, M. L., *Prog. Rept.* 63, Penn. State Coll., Agr. Exp. Sta., State College, Penna., January, 1952.
- (46) Beamer, P. R., *Ann. N.Y. Acad. Sci.*, **55**, 1209 (1952).
- (47) Blake, F. G., *The Present Status of Antibiotics Therapy with Particular Reference to Chloramphenicol, Aureomycin, and Terramycin*, Thomas, Springfield, Ill., 1952.
- (48) Brainerd, H. D., Bryn, H. B., Jr., Meiklejohn, G., and Scaparone, M., *Proc. Soc. Exptl. Biol. & Med.*, **70**, 318 (1949).
- (49) Braley, A. E., and Sanders, M., *J. Am. Med. Assoc.*, **138**, 426 (1948).
- (50) Bryer, M. S., Schoenbach, E. B., Bliss, E. A., and Chandler, C. A., *Ann. N.Y. Acad. Sci.*, **51**, 254 (1948).
- (51) Bryer, M. S., Schoenbach, E. B., Chandler, C. A., Bliss, E. A., and Long, P. H., *J. Am. Med. Assoc.*, **138**, 117 (1948).
- (52) Buchman, J., *Bull. Hosp. Joint Diseases*, **11**, 156 (1950).
- (53) Chandler, C. A., and Bliss, E. A., *Ann. N.Y. Acad. Sci.*, **51**, 221 (1948).
- (54) Chen, C. H., Dienst, R. B., and Greenblatt, R. B., *J. Am. Med. Assoc.*, **39**, 237 (1950).
- (55) Chivers, W. H., *J. Am. Vet. Med. Assoc.*, **120**, 31 (1952).
- (56) Cipes, L. R., *N.Y. Dental J.*, **16**, 450 (1950).
- (57) Coates, M. E., Dickinson, D. C., Harrison, G. F., Kon, S. K., Porter, J. W. G., Cummins, S. H., and Cuthbertson, W. F. J., *J. Sci. Food Agr.*, **3**, 43 (1952).
- (58) Coffey, G. L., Schwab, J. L., and Ehrlich, J., *J. Infectious Diseases*, **87**, 142 (1950).
- (59) Collins, H. S., Paine, T. F., Jr., and Finland, M., *Ann. N.Y. Acad. Sci.*, **51**, 231 (1948).
- (59a) Cooper, W. C., Coatney, G. R., Imboden, C. A., Jr., and Jeffery, G. M., *Proc. Soc. Exptl. Biol. Med.*, **72**, 587 (1949).
- (60) Reed, J. R., and Couch, J. R., *Poultry Sci.*, **29**, 468 (1950).
- (61) Crile, G., and Turnbull, R. B., *J. Iowa State Med. Soc.*, **42**, 12 (1952).
- (62) Cunha, T. J., Burnside, J. E., Buchanan, D. M., Glascock, R. S., Pearson, A. M., and Shealy, A. L., *Arch. Biochem.*, **23**, 324 (1949).
- (63) Dall, E. R., McGee, W. R., *Vet. Med.*, **46**, 123 (1951).
- (64) Dearing, W. H., and Heilman, J. R., *Gastroenterology*, **16**, 12 (1950).
- (65) Dearing, W. H., and Heilman, J. R., *Proc. Staff Meetings Mayo Clinic*, **28**, 121 (1953).
- (66) Dornbush, A. C., and Pelcak, E. J., *Ann. N.Y. Acad. Sci.*, **51**, 218 (1948).
- (67) Dowling, H. F., *Med. Ann. Dist. Columbia*, **28**, 335 (1949).
- (68) Dowling, H. F., Lepper, M. H., Sweet, L. K., and Brickhouse, R. L., *Ann. N.Y. Acad. Sci.*, **50**, 241 (1948).
- (69) Easterbrook, H. L., *J. Am. Vet. Med. Assoc.*, **116**, 48 (1950).
- (70) Editorial, *New Engl. J. Med.*, **249**, 37 (1953).
- (71) Egan, G. F., *J. Oral Surg.*, **8**, 60 (1950).
- (72) Everett, F. G., *J. Am. Dental Assoc.*, **40**, 555 (1950).
- (73) *Federal Register*, 1954.
- (74) Goldman, H. M., and Bloom, J., *Oral Surg., Oral Med. Oral Pathol.*, **2**, 1128 (1949).
- (75) Goldman, H. M., and Bloom, J., *Oral Surg., Oral Med. Oral Pathol.*, **3**, 1148 (1950).
- (76) Gray, M. L., and Moore, G. R., *North Am. Veterinarian*, **34**, 99 (1953).
- (77) Greenspan, R., MacLean, H., Milzer, A., and Neeheles, H., *Am. J. Digest Diseases*, **18**, 35 (1951).
- (78) Hammond, J. C., and Titus, H. W., *Poultry Sci.*, **23**, 49 (1944).
- (79) Harms, H. F., Harms, H. F., Jr., and Harms, G. R., *J. Am. Vet. Med. Assoc.*, **117**, 462 (1950).
- (80) Harned, B. K., Cunningham, R. W., Clark, M. C., Cosgrove, R., Hine, C. H., McCauley, W. J.,

- Stokey, E., Vessey, R. E., Yuda, N. N., and Subbarow, Y., *Ann. N.Y. Acad. Sci.*, **51**, 182 (1948).
- (81) Herrell, W. E., *Am. J. Med. Sci.*, **219**, 570 (1950).
- (82) Herrell, W. E., and Heilman, F. R., *Proc. Staff Meetings Mayo Clinic*, **24**, 157 (1949).
- (83) Hewitt, R., Wallace, W., and White, E., *Science*, **112**, 144 (1950).
- (84) Hiseox, D. J., *J. Am. Pharm. Assoc.*, **40**, 237 (1951).
- (85) Hoffman, M. S., Wellman, W. E., and Herrell, W. E., *Proc. Staff Meetings Mayo Clinic*, **25**, 463 (1950).
- (86) Knight, V., Ruiz-Sanchez, F., Ruiz-Sanchez, A., and McDermott, W., *Am. J. Med.*, **6**, 407 (1949).
- (87) Krider, J. L., personal communication, 1950.
- (88) Lennette, E. H., Meiklejohn, G., and Thelen, H. M., *Ann. N.Y. Acad. Sci.*, **51**, 331 (1948).
- (89) Lepage, F., Granjon, A., and Culioli, R., *Bull. assoc. gynéc. et obstét. langue franç.*, **2**, 564 (1950).
- (90) Lepper, M. H., Dowling, H. F., Brickhouse, R. L., and Caldwell, E. R., Jr., *J. Lab. Clin. Med.*, **34**, 366 (1949).
- (91) Lepper, M. H., Wolfe, C. K., Zimmerman, H. J., Caldwell, E. R., Spies, H. W., and Dowling, H. F., *Arch. Internal Med.*, **88**, 271 (1951).
- (92) Levine, J., Garlock, E. A., Jr., and Fischbach, H., *J. Am. Pharm. Assoc., Sci. Ed.*, **38**, 473 (1949).
- (93) Logan, M. A., Metzger, W. I., Wright, L. T., Prigot, A., and Robinson, E. A., *Am. J. Surg.*, **79**, 229 (1950).
- (94) Long, P. H., *Bull. N.Y. Acad. Med.*, **28**, 809 (1952).
- (95) Long, P. H., Bliss, E. A., Schoenbach, E. B., Chandler, C. A., and Bryer, M. S., *Lancet*, **1**, 1139 (1950).
- (96) Loosli, J. K., and Wallace, H. D., *Proc. Soc. Exptl. Biol. Med.*, **75**, 531 (1950).
- (97) Loughlin, E. H., Joseph, H., and Schaefer, K., *Am. J. Trop. Med.*, **31**, 20 (1951).
- (98) Lower, H. C., *North Am. Veterinarian*, **31**, 800 (1950).
- (99) McGinnis, J., Stephenson, E. L., Lavadie, B. T., Carver, J. S., Garibaldi, J. A., Ijichi, K., Snell, N. S., and Lewis, J. C., "Response of Chicks and Turkey Poults to Vitamin B<sub>12</sub> Supplements Produced by Fermentation with Different Organisms," *Abstracts of Papers, 116th Meeting Am. Chem. Soc. (Atlantic City, N.J.), Sept. 1949*, p. 42A.
- (100) McGinnis, J., Stevens, J. M., and Groves, K., *Poultry Sci.*, **26**, 432 (1947).
- (101) McVay, L. V., Laird, R. L., and Sprunt, D. H., *Science*, **109**, 590 (1949).
- (102) McVay, L. V., Jr., Laird, R. L., and Sprunt, D. H., *Southern Med. J.*, **43**, 308 (1950).
- (103) McVay, L. V., Jr., and Sprunt, D. H., *Ann. Internal Med.*, **38**, 955 (1953).
- (104) Meiklejohn, G., and Schragg, R. I., *J. Am. Med. Assoc.*, **140**, 139 (1949).
- (105) Metzger, W. I., Wright, L. T., De Fua, L. R., Jard, C. E., and Katske, F., *J. Urol.*, **67**, 374 (1952).
- (106) Monnier, J. J., and Schoenbach, E. B., *Antibiotics & Chemotherapy*, **1**, 472 (1951).
- (107) Paine, T. F., Jr., Collins, H. S., and Finland, H., *Ann. N.Y. Acad. Sci.*, **51**, 228 (1948).
- (108) Perrini, F., *Boll. soc. ital. biol. sper.*, **27**, 1151 (1951).
- (109) Price, C. W., Randall, W. A., and Welch, H., *Ann. N.Y. Acad. Sci.*, **51**, 211 (1948).
- (110) *Product Descriptions*, Lederle Laboratories Division and Fine Chemicals Division, Pearl River, N.Y., 1954, pp. 17-33.
- (111) Pulaski, E. J., Artz, C. P., and Riess, E., *J. Am. Med. Assoc.*, **148**, 165 (1952).
- (112) Ransmeier, J. C., *J. Clin. Invest.*, **28**, 997 (1949).
- (113) Riekas, E. L., Brink, N. G., Koniuszy, F. R., Wood, T. R., and Folkers, K., *Science*, **108**, 634 (1948).
- (114) Robinson, P., *Lancet*, **1**, 52 (1952).
- (115) Rodriguez, J., Plotke, J., Weinstein, S., and Harris, W. W., *J. Am. Med. Assoc.*, **141**, 771 (1949).
- (116) Ross, S., Burke, J. G., Rice, E. C., Schoenbach, E. B., Bischoff, H., and Washington, J. A., *Clin. Proc. Child. Hosp. (Washington, D.C.)*, **4**, 215 (1948).
- (117) Ross, S., Bischoff, H., Preisser, W., and Orr, W. (Abstract), *J. Clin. Invest.*, **28**, 1050 (1949).
- (118) Ross, S., Schoenbach, E. B., Burke, J. G., Bryer, M. S., Rice, E. C., and Washington, J. A., *J. Am. Med. Assoc.*, **138**, 1213 (1948).
- (119) Roth, L. H., *J. Ohio Dental Assoc.*, **26**, 58 (May, 1952).
- (120) Roelstad, G. H., *J. Am. Dental Assoc.*, **43**, 52 (1951).
- (121) Rubin, M., and Bird, H. R., *J. Biol. Chem.*, **163**, 387 (1946).

- (122) Rubin, M., Bird, H. R., and Rothchild, I., *Poultry Sci.*, **25**, 526 (1946).
- (123) Rutenburg, A. M., Jacob, S. W., Schweinburg, F. B., and Fine, J., *New Engl. J. Med.*, **246**, 52 (1952).
- (124) Rutenburg, A. M., and Schweinburg, F. B., *Proc. Soc. Exptl. Biol. Med.*, **70**, 464 (1949).
- (124a) Saz, A. K., and Slie, R. B., *Bacteriol. Proc.*, **1954**, 119.
- (125) Schoenbach, E. B., *J. Am. Med. Assoc.*, **139**, 450 (1949).
- (126) Schoenbach, E. B., Bryer, M. S., and Long, P. H., *Ann. N.Y. Acad. Sci.*, **51**, 231 (1948).
- (127) Scrimshaw, N. S., and Guzman, M. A., INCAP Scientific Contribution 1-29., *Proc. Ann. Meeting National Vitamin Foundation*, New York, 1953.
- (128) Shwachman, H., Foley, G. E., and Cook, C. D., *J. Pediat.*, **38**, 91 (1951).
- (129) Singen, E. P., and Matterson, L. D., *Poultry Sci.*, **29**, 468 (1950).
- (130) Slanetz, L. W., and Allen, F. E., *J. Am. Vet. Med. Assoc.*, **117**, 392 (1950).
- (131) Snelling, C. E., and Johnson, R., *Can. Med. Assoc. J.*, **66**, 6 (1952).
- (132) Spink, W. W., Braude, A. I., Ruiz-Castaneda, M., and Silva Goytia, R., *J. Am. Med. Assoc.*, **138**, 1145 (1948).
- (133) Spies, H. W., Dowling, H. R., Lepper, M. H., Wolfe, C. K., and Caldwell, E. R., *Arch. Internal Med.*, **87**, 66 (1951).
- (134) Steenken, W., and Wolinsky, E., *Am. Rev. Tuberc.*, **59**, 221 (1949).
- (135) Stokstad, E. L. R., *Physiol. Revs.*, **34**, 1 (1954).
- (136) Stokstad, E. L. R., Jukes, T. H., Pierce, J., Page, A. C., Jr., and Franklin, A. L., *J. Biol. Chem.*, **180**, 647 (1949).
- (137) Tarr, H. L. A., Boyd, J. W., and Bissett, H. M., *J. Agr. Food Chem.*, **2**, 372 (1954).
- (138) Waletzky, E., unpublished data, American Cyanamid Research Laboratories, Stamford, Conn.
- (139) Weiser, H. H., Kunkle, L. E., and Deatherage, F. E., *Appl. Microbiol.*, **2**, 88 (1954).
- (140) Welch, H., Hendricks, F. D., Price, C. W., and Randall, W. A., *J. Am. Pharm. Assoc., Sci. Ed.*, **39**, 185 (1950).
- (141) Wiggall, R. H., et al., *Am. J. Syphilis*, **33**, 416 (1949).
- (142) Wright, F. T., Sanders, M., Logan, M. A., Prigot, A., and Hill, L. M., *Ann. N.Y. Acad. Sci.*, **51**, 318 (1948).
- (143) Wright, L. T., Sanders, M., Logan, M. A., Prigot, A., and Hill, L. M., *J. Am. Med. Assoc.*, **138**, 408 (1948).

L. M. PRUESS (Properties; Preparation and Manufacture)  
C. H. DEMOS

### OXYTETRACYCLINE

Oxytetracycline, N.N.R. (Terramycin),  $C_{22}H_{24}N_2O_9$  (formula, p. 772), is a pale yellow, crystalline, amphoteric, broad-spectrum antibiotic produced under controlled conditions by a species of actinomycetes, *Streptomyces rimosus* (14,77). The new actinomyceete was isolated from a soil sample as a result of a planned research program and received its name as a consequence of the cracked appearance of its growth on the surface of an agar medium (14). The antibiotic has a marked inhibitory effect against a wide variety of microorganisms including many Gram-positive and Gram-negative bacteria (aerobic and anaerobic), the rickettsia, and certain of the larger viruses (14). Oxytetracycline is commercially available as the amphoteric base and its hydrochloride salt.

**Physical Properties.** Oxytetracycline crystallizes as a dihydrate, m.p. 181–182°C.;  $[\alpha]_D^{25} + 26.5^\circ$  (C, 1% in methanol),  $[\alpha]_D^{25} - 196.6^\circ$  (C, 1% in 0.1 N hydrochloric acid),  $[\alpha]_D^{25} - 2.1^\circ$  (C, 1% in 0.1 N sodium hydroxide). It is very soluble in acids and alkalies, very slightly soluble in acetone, ethyl alcohol, chloroform, and water, and practically insoluble in ether. The dihydrate crystals are biaxial negative with parallel extinction and have the refractive indexes (54)  $\alpha = 1.634 \pm 0.004$ ,

$\beta = 1.646 \pm 0.004$ , and  $\gamma = >1.70$ . The dihydrate loses its water of crystallization on heating *in vacuo* at  $100^\circ\text{C}$ . The molecular weight of the anhydrous substance as given by x-ray data (56) is  $462.5 \pm 5$ , m.p.  $184.5\text{--}185.5^\circ\text{C}$ . (decompn.). Its optical rotation is sensitive to pH and strongly affected by boric acid.

The ultraviolet absorption spectra of oxytetracycline and of oxytetracycline hydrochloride in methanol solutions are very similar but somewhat different from that of the sodium salt: oxytetracycline in methanol,  $E_{1\%}^{1\text{cm.}} = 361$  (270  $m\mu$ ), 343 (370  $m\mu$ ); oxytetracycline in 0.01 *N* methanolic hydrochloric acid,  $E_{1\%}^{1\text{cm.}} = 353$  (270  $m\mu$ ), 267 (359  $m\mu$ ); oxytetracycline in 0.01 *N* methanolic sodium hydroxide,  $E_{1\%}^{1\text{cm.}} = 415$  (245  $m\mu$ ), 405 (264  $m\mu$ ), 352 (375  $m\mu$ ) (55). The infrared spectra of oxytetracycline dihydrate and oxytetracycline hydrochloride in Nujol mulls are not greatly different. The infrared spectra show no bands below  $5.9\ \mu$  and thus exclude the presence within the molecule of simple unconjugated aldehyde, ketone, carboxylic acid, ester, and lactone functions (26).

**Chemical Properties.** Oxytetracycline gives positive ferric chloride, Pauley, Friedel-Crafts, Fehling, and Molisch tests (54).

Oxytetracycline readily forms well-defined salts with both acids and bases. The hydrochloride and hydrobromide are, for example, well-characterized, bright yellow, beautifully crystalline salts. The hydrohalides dissolve readily in water, but, unless excess acid is added to a pH below 1.5, the crystalline amphoteric substance separates on standing.

*Oxytetracycline hydrochloride*,  $\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_9 \cdot \text{HCl}$ , N.N.R., is a yellow, crystalline, odorless powder with a bitter taste, m.p.  $190\text{--}194^\circ\text{C}$ . (decompn.). It is very soluble in water (with the qualifications noted above), soluble in ethyl alcohol, sparingly soluble in acetone, slightly soluble in chloroform, and very slightly soluble in benzene and ether. A 1% solution of the hydrochloride has a pH of about 2.5. It crystallizes from methanol in the form of needles. It can be recrystallized from water at  $50^\circ\text{C}$ . in the form of platelets. (At this temperature the solubility of the dihydrate is greater than that of the hydrochloride.)

The disodium and dipotassium salts of oxytetracycline are yellow crystalline hydrates which are readily soluble in water and insoluble in alcohol. The sodium salt,  $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}_9 \cdot \text{Na}_2 \cdot 2\text{H}_2\text{O}$ , crystallizes from methanol. The calcium and magnesium salts of oxytetracycline are only slightly soluble in water (55).

Oxytetracycline readily forms mixed salts with a number of pairs of bivalent metal ions. The barium-calcium and barium-magnesium salts are very insoluble in water and precipitate readily from aqueous solutions at pH 8.5–9.5. In addition, oxytetracycline has a marked tendency to form complexes with certain inorganic salts. For example, the pH of an aqueous solution of oxytetracycline shifts almost two units upon the addition of one mole of calcium chloride. Several complexes of oxytetracycline and calcium chloride exist in solution. A crystalline complex has been isolated having a composition in fairly good agreement with the formula  $(\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_9)_4 \cdot \text{CaCl}_2$  (55).

The unique structure for oxytetracycline (p. 772) is delineated in one general paper, which formed the basis for structure proofs of chlortetracycline and tetracycline (26; see also p. 787, ref. 26; p. 809, ref. 26a). Only the significant reactions of oxytetracycline and its degradation products observed during the course of structural studies will be given here.

Structural determinations revealed the antibiotic to be a new type of chemical substance, 4-dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12,12a-hexahydroxy-6-methyl-1,11-dioxo-2-naphthacene-carboxamide.

The antibiotic possesses eight active hydrogens, but only two can be identified as

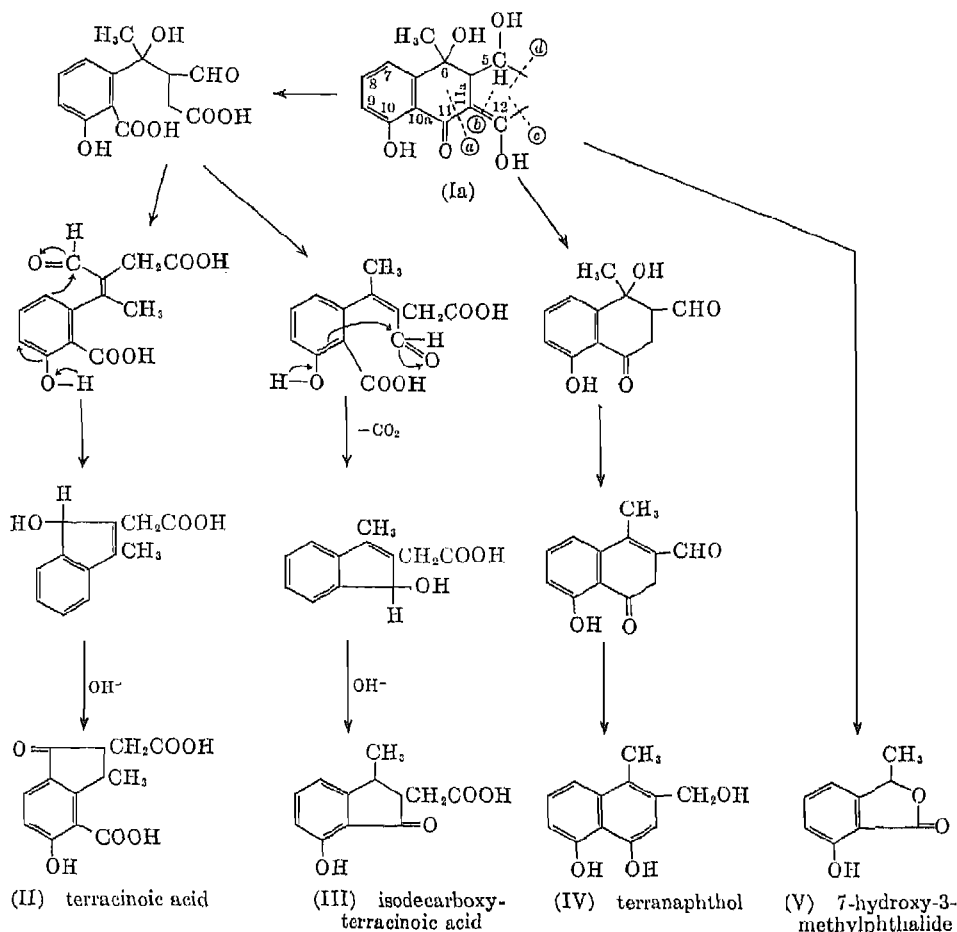
titrable groups. In aqueous solution oxytetracycline hydrochloride exhibits  $pK_a$  values of 3.5, 7.6, and 9.2. Two of these acid functions are involved in the formation of dimethyloxytetracycline whose hydrochloride gives a  $pK_a$  of 7.7.

*Action of Alkali.* Since the infrared spectrum of oxytetracycline shows no evidence of carboxylic functions, the two acidic hydrogens are regarded as being associated with phenolic or enolic functions as indicated by the positive ferric chloride test given by oxytetracycline and by the isolation, from alkali fusion, of salicylic acid, *m*-hydroxybenzoic acid (46,48), and 6-acetylsalicylic acid (33), in addition to acetic and succinic acids.

The action of hot aqueous alkali on oxytetracycline liberates one mole each of dimethylamine and ammonia (46).

When oxytetracycline is digested in aqueous alkali in the presence of zinc, the resultant compounds are the end products of alternative modes of decomposition of the same portion of the oxytetracycline structure (Ia, see Scheme 1) (25,26,47). The following is a reaction sequence which would allow for the products obtained. If

SCHEME 1



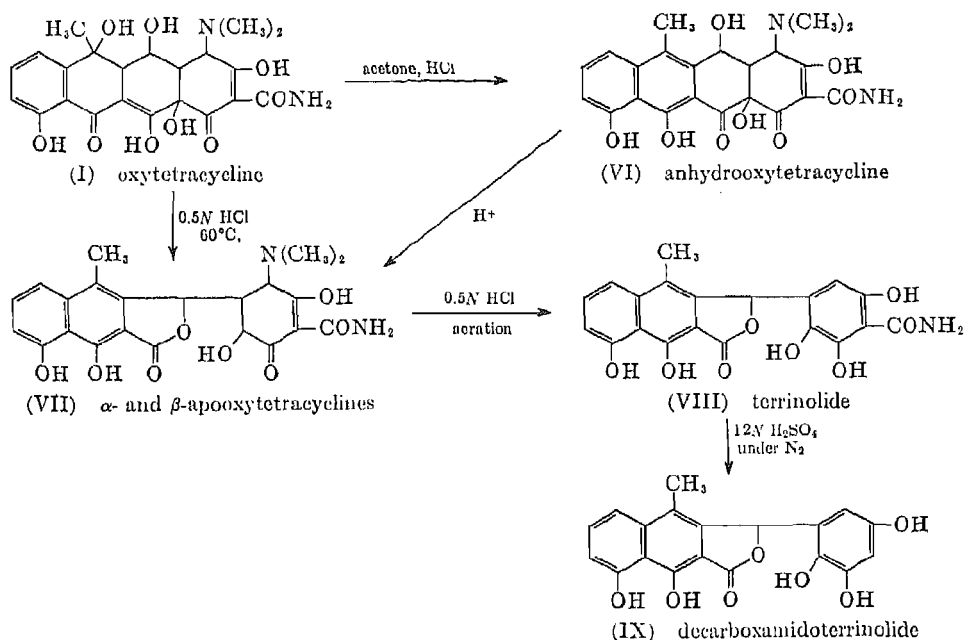


bonds *a*, *c*, and *d* are cleaved, dehydration at C-6 results in an unstable, primary nonasymmetric precursor and is followed by bond formation (C-5  $\rightarrow$  C-7) to give a new five-membered carbocyclic ring. In the presence of a base this compound is converted to a well-defined, racemic crystalline acid, **terracinoic acid** (4-carboxy-5-hydroxy-3-methylindanone-2-acetic acid, II). An alternative cyclization (C-5  $\rightarrow$  C-10a) followed by decarboxylation yields **isodecarboxyterracinoic acid** (7-hydroxy-3-methylindanone-2-acetic acid, III).

Cleavage of bonds *b* and *d* liberates an aldehyde function at C-5. Loss of water at C-6 by a base-catalyzed elimination is followed by aromatization and reduction by zinc to form **terrannaphthol** (3-hydroxymethyl-4-methyl-1,8-naphthalenediol, IV). 7-Hydroxy-3-methylphthalide (V) is also found among the alkaline degradation products.

*Action of Acid.* Oxytetracycline undergoes stepwise degradation (see Scheme 2) with successively stronger acids. Each product is related simply to its precursor. Since the C-12 hydroxyl hydrogen of oxytetracycline is capable of enolization with the carbonyl (oxo group) at C-11 and the tertiary hydroxyl group at C-6 situated  $\alpha$  to the aromatic ring is subject to acid-catalyzed dehydration, all the acid degradation products possess the naphthalene system and all but **anhydrooxytetracycline** (VI) contain it as the 8,9-dihydroxybenzophthalide system.

SCHEME 2

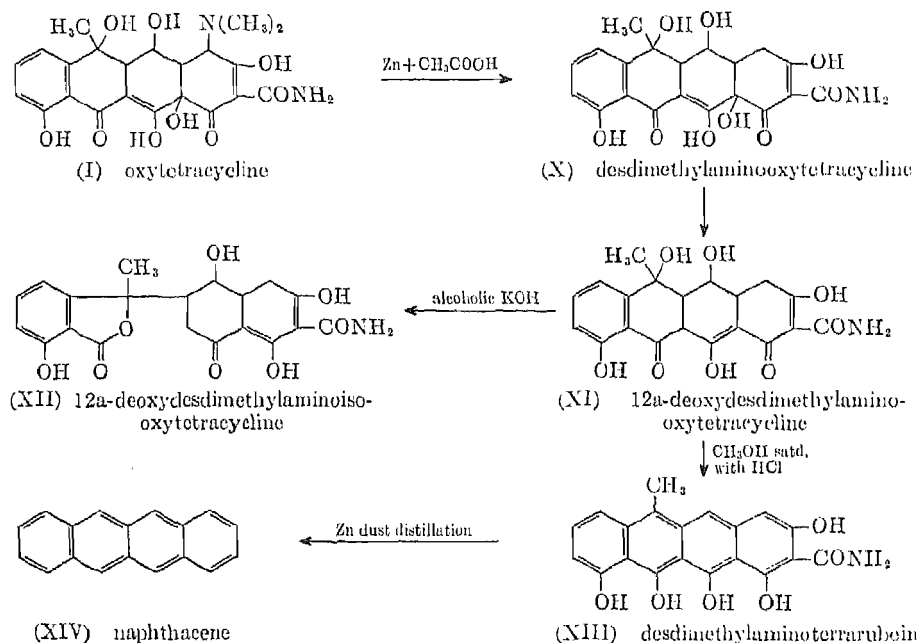


Alkali fusion of the **apooxytetracyclines** (VII) yields 4,5-dihydroxy-1-methyl-2,3-naphthalenedicarboxylic acid and 2,5-dihydroxybenzoquinone. Isolation of the latter compound was of great significance in the ultimate interpretation of the groupings attached to ring A of the oxytetracycline molecule.

*Reductive Degradation.* As shown in Scheme 3, reductive degradation also pro-

vides a distinct series of products which were of particular value in connection with structural studies. Under mild action of zinc and acetic acid, dimethylamine is split from oxytetracycline to give **desdimethylaminooxytetracycline** (X). Continued prolonged action of zinc and acetic acid causes further loss of an oxygen atom at C-12a leading to **12a-deoxydesdimethylaminooxytetracycline** (XI). In alkali, deoxydesdimethylaminooxytetracycline is smoothly isomerized through hydrolytic cleavage at C-11a and phthalide formation to **12a-deoxydesdimethylaminoisooxytetracycline** (XII). However, under mild acid conditions (XI) loses two molecules of water, resulting in a highly soluble orange-red compound, **desdimethylaminoterrarubein** (XIII), containing a totally aromatic and conjugated system. Zinc-dust distillation of (XIII) yields the aromatic hydrocarbon **naphthacene** (XIV). This last series of reactions established the linear tetracyclic structure.

SCHEME 3



Of the degradation products shown in Schemes 1-3, only anhydrooxytetracycline (VI) and deoxydesdimethylaminooxytetracycline (XI) exhibit slight antibacterial activity (53).

Several derivatives of oxytetracycline have been prepared, for example, a dimethyl ether, a diacetyl derivative, and a benzensulfonyl derivative in which the carboxamide group at C-2 is also modified to a nitrile (26).

### Preparation and Manufacture

An inoculum of *S. rimosus* may be obtained by employing a growth from slants or Roux bottles previously inoculated with this organism. A solid medium suitable for this initial growth is beef lactose or Emerson's agar. This growth is used to inoculate submerged inoculum tanks in which it reaches maximum growth within 2 days.

*S. rimosus* grows preferably at 24–30°C. under submerged conditions of agitation and aeration (4,8,77). Conditions for growth of the actinomycete are best carried out in media consisting of a carbohydrate source, such as a sugar, starch, glycerol; an organic nitrogen source, such as soybean meal, wheat gluten, cottonseed meal, lactalbumin, tryptone (an enzymatic digest of casein); a source of growth substances, such as distillers' solubles, yeast extract; mineral salts, such as sodium chloride, potassium phosphate, magnesium sulfate, sodium nitrate; a buffering agent, such as calcium carbonate; and a vegetable oil.

From the inoculum tank the broth containing the microorganism is forced into the fermentor under completely aseptic conditions, and growth is continued for 4 days. At all times aeration is maintained in the vigorously stirred both by blowing in sterile air through a sparger at the rate of  $\frac{1}{2}$  to 2 volumes of free air per volume of broth per minute. Foaming is usually controlled by the addition of vegetable or animal oils.

In the large-scale production of oxytetracycline the inoculum is prepared in a large tank containing 1 part enzymatic digest of casein (N-Z-Amine B), 1 part Cerelese, 0.5 part yeast extract, 0.5 part sodium chloride, 0.1 part calcium carbonate, and 96.9 parts water. The medium is adjusted to pH 6.7 with potassium hydroxide and sterilized by heating at 121°C. for 1 hr. After cooling to 28°C., the medium is inoculated with a suspension of *S. rimosus*. The tank is aerated and agitated for 25 hr. and the contents then used to inoculate the fermentor. The large-scale fermentor contains a medium composed of 3 parts soybean meal, 0.5 part corn starch, 0.1 part N-Z-Amine B, 0.3 part sodium nitrate, 0.5 part calcium carbonate, and 0.4 part vegetable oil in tap water and adjusted to pH 7.0. The whole mixture is sterilized by heating at 121°C. for 1 hr. After cooling to 28°C., the tank is inoculated with the contents of the inoculum vessel. In general, the same type of equipment that is used for penicillin fermentation (4,8) with respect to agitation and aeration is also satisfactory for the oxytetracycline fermentation. At the end of 47 hr. at 28°C. the potency reaches a maximum of about 1000  $\gamma$ /ml. (30,55), the pH rises to 8.0, and the fermentation is ready for harvest (77).

**Extraction and Purification.** The solubility of oxytetracycline and its hydrochloride salt provides several methods for its isolation and purification. Oxytetracycline may be extracted with 1-butanol from alkaline solutions (77) or by a variety of solvents with the aid of sequestering agents added to dilute solutions of oxytetracycline (79). The antibiotic may be precipitated from fermentation broths by certain pairs of multivalent metal ions, such as barium and magnesium (55). In addition, the antibiotic can be precipitated from dilute aqueous solutions by the addition of a variety of arylazosulfonic acid dyes (78) or by the addition of quaternary ammonium salts (12).

In actual practice one of the methods (55,76) for recovering the antibiotic involves acidification of the fermentation broth to pH 2.5 with sulfuric acid, after which the mycelia are removed in the presence of large quantities of filter aids. The filtrate is treated during a half-hour period with a solution containing barium chloride dihydrate and magnesium chloride hexahydrate in the ratio 15.5:2.07 per part of oxytetracycline in solution. The mixture of inorganic salts of oxytetracycline is adjusted to pH 8.5 by slow addition of 10% sodium hydroxide, and the precipitate of the barium-magnesium-oxytetracycline complex is recovered over filter aids. The filtrates show about 7–10% loss of antibiotic. The washed filter cakes are suspended in water, and the mixture is acidified to pH 1.5 with 50% sulfuric acid. After vigorous stirring, the

filter aid and the precipitated barium sulfate are separated by filtration. The precipitates are usually re-extracted with dilute sulfuric acid, and the combined filtrates are adjusted to pH 3.0 with 10% sodium hydroxide. The precipitation of oxytetracycline is accelerated by slow additions of sodium hydroxide to pH 7.0. The crude amphoteric oxytetracycline is filtered and washed with water. The base is purified by conversion to the hydrochloride salt, which is then dissolved in water. The pH of the solution is adjusted to 7, and the pure base is collected and washed.

Pure oxytetracycline hydrochloride is prepared from crude preparations by solution in methanol. A saturated solution of calcium chloride in methanol is then added with stirring. After  $\frac{1}{2}$  hr., adsorbent charcoal (Darco-G60) is added, the solution is filtered over filter aids, and the cake is washed with a saturated methanolic solution of calcium chloride, 1.5 *N* methanolic hydrochloric acid, and finally with anhydrous methanol. Concentrated hydrochloric acid is added slowly to the combined filtrate and washes containing the oxytetracycline, and after stirring for 1 hr. the crystals are collected and washed with 1.5 *N* methanolic hydrochloric acid followed by anhydrous methanol. The oxytetracycline hydrochloride thus obtained is recrystallized by suspension in methanol and treatment with triethylamine to convert oxytetracycline hydrochloride to the amphoteric base. Calcium chloride is added to produce a clear solution, and Darco-G60 is added to this mixture. After filtration the filtrate is treated with concentrated hydrochloric acid and stirred for  $\frac{1}{2}$  hr. Pure oxytetracycline hydrochloride is collected by filtration and dried at 50°C. *in vacuo*. The pure anhydrous antibiotic obtained in this way is made available for oral use.

**Market Forms.** Oxytetracycline is available in a variety of dosage forms. For oral purposes capsules are most widely used, but sugar-coated tablets and flavored oral suspensions of the antibiotic are also utilized. An intramuscular dosage form composed of a sterile, pyrogen-free, dry mixture of crystalline oxytetracycline hydrochloride, magnesium hydrochloride, and procaine hydrochloride (7,34) is available for patients for whom the oral route is not recommended. For hospitalized patients an intravenous form is administered which is made up of oxytetracycline hydrochloride and sodium glycinate buffer at pH 9.0 (29). Several ointments are available for topical and ophthalmic applications. Several other forms are available for specific purposes: dental paste, dental cones, vaginal suppositories, nasal solutions, otic solutions, aerosol solutions, topical powder, and impregnated gauze pads.

TABLE I. The Stability of Oxytetracycline at 37°C. as a Function of pH.

pH	Half-life, hr.
1.0.....	114
2.5.....	134
4.6.....	45
5.5.....	45
7.0.....	26
8.5.....	33
10.0.....	14

**Stability.** In the dry crystalline state, oxytetracycline and its hydrochloride show no detectable loss in biological potency on prolonged storage at room temperature. Even when the hydrochloride is maintained at 50°C. for 4 months, less than 5% inactivation is observed. No loss in potency of oxytetracycline base is noted during 4

days of heating at 100°C. The stability of oxytetracycline solutions is given in Table I (54).

### Microbiological Properties

**Antimicrobial Activity.** Oxytetracycline gave immediate evidence of being a useful antibiotic with wide clinical potentialities when it was found that concentrations of 1-3  $\gamma$ /ml. were effective against strains of *Aerobacter aerogenes*, *Klebsiella pneumoniae*, *Salmonella typhosa*, *Salmonella paratyphi*, *Salmonella schottmuelleri*, *Salmonella pullorum*, *Shigella paradysenteriae*, *Bacillus subtilis*, *Staphylococcus albus*, *Staphylococcus aureus*, and *Brucella bronchiseptica*. The drug was found to be effective against certain strains of *Pseudomonas aeruginosa* (13) and *Escherichia coli* but not against a species of *Proteus* (14).

Further work by other investigators (16,23,24,31,68) emphasized the antimicrobial activity of oxytetracycline against a wide variety of aerobic and anaerobic Gram-positive and Gram-negative bacteria, certain rickettsiae, and against viruses of the psittacosis-lymphogranuloma groups. In addition, 5-10  $\gamma$ /ml. of oxytetracycline was found to inhibit the growth of the H37Rv strain of the tubercle bacillus. The streptomycin-resistant strain of this microorganism was shown to be as sensitive to oxytetracycline as the streptomycin-sensitive strain is (65). Moreover, the drug is quite active against the clostridia and saprophytic mycobacteria (68). Oxytetracycline has been shown to have marked antirickettsial properties. The drug has been used successfully against the rickettsiae of epidemic and murine typhus, Rocky Mountain spotted fever, rickettsial pox, scrub typhus, etc. (5,57,63,64). The antibiotic, however, is inactive against yeast-like organisms and *Proteus vulgaris*.

Oxytetracycline is an antimicrobial agent which acts promptly on sensitive cells and exerts a bactericidal effect only when it is present in high concentrations relative to the number of microorganisms (24). When this ratio diminishes, as it usually does in clinical therapy, the drug possesses largely a bacteriostatic effect rather than a bactericidal one (24,68). The mode of action of oxytetracycline has been investigated (70a) (see p. 773).

The range of sensitivities to oxytetracycline of a group of selected organisms has been summarized (69).

**Development of Resistance.** The increase in resistance to oxytetracycline by transfers in media containing increasing concentrations of the drug is gained slowly in a gradual, stepwise fashion. This pattern of resistance is comparable to that of other broad-spectrum antibiotics and is in marked contrast to that of streptomycin. With certain strains of *Staphylococcus*, *Enterococcus*, and *Streptococcus viridans*, resistance to oxytetracycline develops to a lower degree than to penicillin (73).

In man, the frequency and rate of emergence of microbial resistance varies with the species of microorganism concerned and the nature of the lesion. Emergence of drug resistance has been reported in occasional instances among strains of staphylococci, enterococci, and nonhemolytic streptococci isolated from patients with subacute bacterial endocarditis. However, emergence of resistance to oxytetracycline has never been observed among strains of pneumococci, hemolytic streptococci, and other pathogenic microorganisms with fastidious growth requirements (22,39).

A change in flora resulting from administration of antimicrobial agents such as oxytetracycline occasionally results in the appearance of resistant microorganisms within the host during therapy. Although microorganisms may be newly introduced into the host and/or may increase to predominant numbers as a result of antimicrobial

therapy, the frequency with which these organisms appear to be pathogenic is low. Indeed, in those few instances in which pathogenicity seems to have occurred, systemic invasion by these organisms frequently has been associated with surgical intervention. Thus it seems probable that some alteration may occur during surgery that is essential for the entry of the organisms into the body and for subsequent development of generalized infection (69).

### Pharmacological Properties

**Absorption and Excretion.** Animal studies indicate that oxytetracycline is widely distributed in the tissues (67).

In human beings, oxytetracycline is readily absorbed from the gastrointestinal tract. Significant and continuous blood concentrations are obtained when 250 mg. is given every 6 hrs. (68). A dose of 0.5 or 1.0 g. of oxytetracycline every 6 hr. will maintain a clinically effective concentration in the serum (10). Patients who received 1 g. every 6 hr. maintained levels of 5–10  $\gamma$ /ml. throughout 24 hr. (60).

Intravenous administration of only 250 mg. of the antibiotic produces serum levels of 5–10  $\gamma$ /ml. at the end of 1 hr. (60), and in addition it is widely distributed in body fluids, organs, and tissues (3,67). Clinically significant serum levels were obtained also with intramuscular preparations in dosages of 100 mg. every 6 hr. (7,34,42).

Oxytetracycline diffuses into the pleural and abdominal fluids and passes the placental barrier easily, being detected in fetal blood or cord blood in concentrations about 25% of that in maternal blood (20,61,70). Though its concentration in spinal fluid of normal subjects varies (20), it may reach significant levels particularly if the meninges are inflamed (51). Measurable concentrations of oxytetracycline were obtained in cerebrospinal fluid (72), in pleural fluid, and in ascites fluid when sufficiently large doses were administered (70).

In man, high concentrations of a biologically active form of oxytetracycline are concentrated in the hepatic system and excreted in bile (20,61,67,68). The antibiotic was found to accumulate in the reticuloendothelial system and to show high concentrations in the liver and kidney, where it is excreted (19,20). Lower concentrations seem to occur in the muscular, bone, and nervous tissues (19).

Oxytetracycline has been found also in high concentrations in human skin, averaging 70% of the corresponding serum levels (18).

Oxytetracycline is readily excreted by the kidneys and appears in the urine in an active state (52,61,68). Excretion of the antibiotic in the urine begins within  $\frac{1}{2}$  hr., and 11–15% of the total dose can be recovered within 24 hr. (11,61). The high concentrations of biologically active oxytetracycline in the urine are of significance in the treatment of urinary tract infections; with a dose of 0.5 g., concentrations of 140  $\gamma$ /ml. were obtained; with 2 g., 400  $\gamma$ /ml. of urine (67,68). There is no evidence that renal dysfunction interferes with the excretion (3). Relatively large amounts of the drug are found in the stool (20,61,67,68), approximately 600  $\gamma$ /g. having been recovered after a dose of 0.5 g. of oxytetracycline (67). The high concentration of the drug in the feces results in some alteration of the bacterial flora in the intestinal tract (20).

Oxytetracycline is excreted in saliva when administered by mouth in capsule form. On an average, salivary excretion lasts for 24 hr. after capsule medication has been discontinued. A 3-g. dose reduces bacterial count in saliva, and the inhibitory effect seems to last for 24 hr. (32).

**Toxicity.** The amphoteric base and the hydrochloride of oxytetracycline show no significant differences in the body (10,28,38), and both forms have shown low toxicity in animal and human studies (24,44,45,61). Oxytetracycline has an oral LD<sub>50</sub> of 6,700 mg./kg. in mice. Daily oral doses of 100–200 mg. of oxytetracycline hydrochloride/kg. of body weight were tolerated by rats during an observation period lasting 8 weeks. Similarly, cats were able to tolerate a daily dose of 186 mg./kg. for a period of 10 weeks, while dogs showed no signs of toxicity at a level of 465 mg./kg. over a period of 57 days. The growth rate of all animals was not adversely affected, and no symptoms of central nervous system irritation appeared even when oxytetracycline was injected intracisternally. The acute intravenous LD<sub>50</sub> of oxytetracycline hydrochloride for mice is 178 mg./kg. of body weight (45). Intravenous injections of the hydrochloride caused no change in blood pressure of anesthetized animals if given slowly (44); and there is only a transient fall on rapid injection. The acute LD<sub>50</sub> of the hydrochloride following subcutaneous injection in mice is 600–650 mg./kg. (61). The antibiotic has no effect on the smooth muscle of isolated intestines or uteri of guinea pigs and rabbits. Furthermore, oxytetracycline does not affect blood sugar (45).

In clinical use, mild gastrointestinal disturbances have been noted in some instances, the most common reaction of which is looseness of the stools although this is not a serious problem (40). These symptoms are diminished if the drug is taken with milk, immediately after meals, or with antacids. Aluminum hydroxide gels given with antibiotics, however, have been shown to decrease absorption and are contraindicated (49). On prolonged therapy there have been reports of glossitis, dermatitis, and pruritis ani and vulvae, but these reactions are quite uncommon.

The gastrointestinal tract irritation due to oxytetracycline, however, is not a serious problem. In one clinical study no patient had to have the drug discontinued on a dosage of 5 g. administered orally during a period of 4 months (40).

Because oral administration of oxytetracycline suppresses growth of bacteria in the intestine, its use may occasionally allow an overgrowth of nonsusceptible organisms, such as monilia, and it may be advisable to administer a vitamin B complex supplement to patients receiving oxytetracycline orally for prolonged periods of time.

The antibiotic is well tolerated by the epithelial membranes and the other tissues of the eye.

**Administration and Dosage.** The dosage of oxytetracycline required to produce the optimum therapeutic response will vary from one patient to another, depending upon the type and severity of infection. The same dosages are recommended for the base and the hydrochloride. The total daily oral dose for moderately ill adults should be based on 25 mg./kg. of body weight. For severely ill adults the total dose is calculated on the basis of 50 mg./kg. of body weight. An initial dose of 2 g. is recommended (10), and appreciable concentrations are maintained up to 24 hr. after a single administration (3,11). The total daily oral dose for infants and children with severe illness is usually based on 40 mg./kg. of body weight (28). It is further recommended that treatment with oxytetracycline should be continued for at least 48 hr. after the patient's temperature has become normal and acute symptoms have subsided.

For systemic distribution of oxytetracycline, the drug is ordinarily given orally in divided doses at 6-hr. intervals (1–4 g. daily depending upon severity and response of infection). An intramuscular dosage form of 100 mg. every 8–12 hr. is prescribed for

patients in whom oral administration is not feasible because of dysphagia, coma, or signs of apparent perforation of the intestinal tract (7). Oxytetracycline for intravenous use can be given subcutaneously with no untoward effects, either local or general (29). For patients with fulminating infections requiring immediate high levels of antibiotic in blood and tissues, notably in peritonitis, 0.25—1 g. every hr. is given by intravenous administration.

### Specification and Assay Method

The Council on Pharmacy and Chemistry (28) recommends a series of identity tests for oxytetracycline: (1) a dark-colored appearance with ferric chloride; (2) a reddish-brown precipitate of copper upon addition of copper tartrate; (3) development of a reddish brown color at the interface upon addition of a solution of 1-naphthol followed by sulfuric acid; (4) the appearance of a red color upon addition of diazobenzenesulfonic acid to an alkaline solution of the antibiotic. The identity tests also include determination of its optical rotation and its absorption maxima at 269 and 353  $m\mu$  and minima at 232 and 299  $m\mu$ . In addition, a series of purity tests is recommended which include infrared spectrum, estimation of heavy metals, loss in weight on drying and residue on ignition, pH of a solution, solubility, and physical appearance. Parenteral products must be sterile (absence of bacteria, molds, yeast, etc.), nontoxic, nonpyrogenic, and free of any depressor substances, such as histamine.

Oxytetracycline is spectrophotometrically determined in a buffer at pH 2.0 at 353  $m\mu$  using the buffer as a blank (21,41). In addition, an effective colorimetric method, which uses ferric chloride after hydrolysis of the antibiotic, has been devised for determining the concentrations of oxytetracycline in solutions containing above 50  $\gamma$ /ml. of oxytetracycline (41). Acid hydrolyzates of the antibiotic can also be estimated by the blue-colored complexes developed by addition of arsenomolybdate reagent (50).

The microbiological assays are carried out by a turbidimetric method (30) using *K. pneumoniae* (A.A.T.C. 10031, P.C.I. 602) and an incubation period of 3.5 hr. Crystalline anhydrous oxytetracycline is used as a standard. The procedure has been applied successfully on both impure and purified preparations of the drug. Moreover, a paper chromatographic test for identity can be employed which is correlated with the bioassay (54). In addition, moderately reliable methods for determination of oxytetracycline in biological fluids have been developed (11).

### Clinical Uses and Indications

Oxytetracycline is effective in the treatment of infections caused by both Gram-positive and Gram-negative bacteria; spirochetes; rickettsiae; pneumonia viruses; and against viruses of the psittacosis-lymphogranuloma groups. Used locally, it is highly effective against *Trichomonas vaginalis* vaginitis.

Human bacterial infections responsive to treatment with oxytetracycline include respiratory tract infections such as sinusitis, tonsillitis, laryngotracheobronchitis, bacterial pneumonias, scarlet fever, bronchiectasis, otitis media and mastoiditis; meningitis; whooping cough; urinary tract infections; gonorrheal infections; infectious arthritis; salmonellosis; bacillary dysentery; tularemia and plague; chancre; brucellosis; listerellosis; bacterial endocarditis and bacteremia; anthrax; intraocular infections; pyrogenic dermatoses; and superficial infections of the nasal



passages, sinuses, external auditory canal, vaginal cavity and cervix, respiratory passages, and external ocular tissues (6,7,15,17,27,35,43,59,62,69,74,75).

Rickettsial diseases in which oxytetracycline has been used with success include typhus, scrub typhus, murine typhus, Rocky Mountain spotted fever, Q fever, boutonneuse fever, and rickettsialpox (69). It is also effective in pinworm infections (9).

Diseases of viral or possible viral etiology in which oxytetracycline has proved effective include primary atypical pneumonia, psittacosis, trachoma, and other viral ocular infections such as inclusion conjunctivitis and follicular conjunctivitis, herpetic gingivostomatitis, granuloma inguinale, venereal lymphogranuloma, and nonspecific urethritis (2,69). Oxytetracycline has also been used with success in cases of actinomyces (69).

Oxytetracycline is used for prophylaxis and treatment of infections of traumatic and surgical wounds (including peritonitis) and puerperal sepsis (7,34,69). As a prophylactic measure in surgery of the large bowel, it is used for the suppression of colonic bacterial flora (69). The antibiotic is prescribed, together with the appropriate surgery, for osteomyelitis and abscesses (69).

Oxytetracycline has also proved useful, in conjunction with streptomycin, in the chemotherapy of tuberculosis, to delay emergence of microbial resistance to streptomycin in patients unable to tolerate *p*-aminosalicylic acid (58) or infected with organisms resistant to it.

Of particular importance in the treatment of patients allergic or unresponsive to penicillin is the effectiveness of oxytetracycline in the spirochetal diseases of syphilis, Vincent's infection, yaws, and infections caused by *Leptospira icterohaemorrhagiae* (36,69). It is also effective, when given internally, in cases of amebiasis (69).

### Bibliography

- (1) Albert, A., *Nature*, **172**, 201 (1953).
- (2) Ambrose, S. S., and Taylor, W. W., *Am. J. Syphilis, Gonorrhea, Venereal Diseases*, **37**, 501 (1953).
- (3) American Medical Association, Council on Pharmacy and Chemistry. *New and Nonofficial Remedies—1954*, J. P. Lippincott Co., Philadelphia.
- (4) Bartholomew, W. H., Karow, E. O., Stat, M. R., and Wilhelm, R. H., *Ind. Eng. Chem.*, **42**, 1801 (1950).
- (5) Bauer, R. E., Parker, R. T., Hall, H. E., Benson, J. F., Joslin, B. S., Hightower, J. A., Snyder, M. J., Venable, S. J., and Woodward, T. E., *Ann. N.Y. Acad. Sci.*, **53**, 395 (1950).
- (6) Bennett, I. L., Russell, P. E., and Derivaux, J. H., *Antibiotics & Chemotherapy*, **2**, 142 (1952).
- (7) Brannick, T. L., Martin, W. J., Geraci, J. E., and Nichols, D. R., *Proc. Staff Meetings Mayo Clinic*, **29**, 183 (1954).
- (8) Brown, W. E., and Peterson, W. H., *Ind. Eng. Chem.*, **42**, 1769 (1950).
- (9) Bumbalo, T. S., and Gustina, F. J., *Postgrad. Med.*, **14**, 83 (1953).
- (10) Caffery, E. I., Alford, B. H., and Musselman, M. M., *Antibiotics & Chemotherapy*, **2**, 72 (1952).
- (11) Carlile, J. D., Kester, A. C., McDonald, C. B., and Clancy, C. F., *J. Am. Pharm. Assoc., Sci. Ed.*, **40**, 535 (1951).
- (12) *Chem. Eng. News*, **29**, 2636 (1951).
- (13) Cutler, M., and Cutler, P., *Am. Practitioner and Dig. Treatment*, **4**, 200 (1953).
- (14) Finlay, A. C., Hobby, G. L., Pan, S. Y., Regna, P. P., Routien, J. B., Seeley, D. B., Shull, G. M., Sobin, B. A., Solomons, I. A., Vinson, J. W., and Kane, J. H., *Science*, **111**, 85 (1950).
- (15) Fleming, S. P., Kearns, P. R., and Lock, F. R., Presented at the Fourth District Interim Session of the American Academy of Obstetrics and Gynecology, Washington, D.C., April 10, 1954.
- (16) Goeke, T. M., Jackson, G. G., Wilcox, C., and Finland, M., *Ann. N.Y. Acad. Sci.*, **53**, 297 (1950).
- (17) Gold, H., and Boger, W. P., *New Engl. J. Med.*, **244**, 391 (1951).
- (18) Gould, J. C., and Ritchie, W. D., *Brit. J. Plastic Surg.*, **5**, 208 (1952).

- (19) Helander, S., and Böttiger, L. E., *Acta. Med. Scand.*, **147**, 71 (1953).
- (20) Herrell, W. E., Heilman, F. R., Wellman, W. E., and Bartholomew, L. G., *Proc. Staff Meetings Mayo Clinic*, **25**, 183 (1950).
- (21) Hiscox, D. J., *J. Am. Pharm. Assoc., Sci. Ed.*, **40**, 237 (1951).
- (22) Hobby, G. L., *Maryland State J. Med.*, in press.
- (23) Hobby, G. L., Dougherty, N., Lenert, T. F., Hudders, E., and Kiseluk, M., *Proc. Soc. Exptl. Biol. Med.*, **73**, 503 (1950).
- (24) Hobby, G. L., Lenert, T. F., Pikula, D., Kiseluk, M., and Hudders, M. E., *Ann. N.Y. Acad. Sci.*, **53**, 266 (1950).
- (25) Hochstein, F. A., and Pasternack, R., *J. Am. Chem. Soc.*, **74**, 3905 (1952).
- (26) Hochstein, F. A., Stephens, C. R., Conover, L. H., Regna, P. P., Pasternack, R., Gordon, P. N., Pilgrim, F. J., Brunings, K. J., and Woodward, R. B., *J. Am. Chem. Soc.*, **75**, 5455 (1953).
- (27) Hoyne, A. L., and Simon, D. L., *Arch. Pediat.*, **70**, 319 (1953).
- (28) *J. Am. Med. Assoc.*, Council on Pharmacy and Chemistry, **151**, 1291 (1953).
- (29) Kagari, B. M., Mendelsohn, R. S., Miller, R. A., and Elegant, L. P., *Antibiotics & Chemotherapy*, **4**, 308 (1954).
- (30) Kersey, R. C., *J. Am. Pharm. Assoc., Sci. Ed.*, **39**, 252 (1950).
- (31) King, E. Q., Lewis, C. N., Welch, H., Clark, E. A., Johnson, J. B., Lyons, J. B., Scott, R. B., and Cornely, P. B., *J. Am. Med. Assoc.*, **143**, 1 (1950).
- (32) Kraus, F. W., Casey, D. W., and Johnson, V., *Proc. Soc. Exptl. Biol. Med.*, **78**, 554 (1951).
- (33) Kuln, R., and Dury, K., *Chem. Ber.*, **84**, 848 (1951).
- (34) Lattarulo, D., Friedman, S., and Bliniek, G., *Antibiotics & Chemotherapy*, **4**, 566 (1954).
- (35) Lenti, G., and Fazio, M., *Minerva med.*, **42**, 195 (1951).
- (36) Liebowitz, D., and Schwartz, H., *J. Am. Med. Assoc.*, **147**, 122 (1951).
- (37) Loomis, W. F., *Science*, **111**, 474 (1950).
- (38) Mason, R., Kice, P., Caffery, E. L., and Musselman, M. M., *J. Am. Pharm. Assoc., Sci. Ed.*, **40**, 587 (1951).
- (39) McDermott, W., and Tomsett, R., personal communication.
- (40) Miller, F. L., and Walker, R., *New Engl. J. Med.*, **249**, 479 (1953).
- (41) Monastero, F., Means, J. A., Grenfell, T. C., and Hedger, F. H., *J. Am. Pharm. Assoc., Sci. Ed.*, **40**, 241 (1951).
- (42) Montmorency, F. A., Caffery, E. L., and Musselman, M. M., *Antibiotics & Chemotherapy*, **4**, 313 (1954).
- (43) Newman, B., Gavis, G., and Weinberg, S., *Antibiotics & Chemotherapy*, in press.
- (44) Pan, S. Y., Reilly, J. C., Halley, T. V., Richard, G. H., Pekiel, A. M., and Pollets, H. A., *J. Pharmacol. Exptl. Therap.*, **99**, 234 (1950).
- (45) Pan, S. Y., Scaduto, L., and Cullen, M., *Ann. N.Y. Acad. Sci.*, **53**, 238 (1950).
- (46) Pasternack, R., Bavley, A., Wagner, R. L., Hochstein, F. A., Regna, P. P., and Brunings, K. J., *J. Am. Chem. Soc.*, **74**, 1926 (1952).
- (47) Pasternack, R., Conover, L. H., Bavley, A., Hochstein, F. A., Hess, G. B., and Brunings, K. J., *J. Am. Chem. Soc.*, **74**, 1928 (1952).
- (48) Pasternack, R., Regna, P. P., Wagner, R. L., Bavley, A., Hochstein, F. A., Gordon, P. N., and Brunings, K. J., *J. Am. Chem. Soc.*, **73**, 2400 (1951).
- (49) Paul, H. E., and Harrington, C. M., *J. Am. Pharm. Assoc., Sci. Ed.*, **41**, 50 (1952).
- (50) Perlman, D., *Science*, **118**, 628 (1953).
- (51) Pulaski, E. J., Artz, C. P., and Reiss, E., *J. Am. Med. Assoc.*, **149**, 35 (1952).
- (52) Purcell, E. M., Wright, S. S., Mou, T. W., and Finland, M., *Proc. Soc. Exptl. Biol. Med.*, **85**, 61 (1954).
- (53) Regna, P. P., *Trans. N.Y. Acad. Sci.*, **15**, 12 (1952).
- (54) Regna, P. P., and Solomons, I. A., *Ann. N.Y. Acad. Sci.*, **53**, 229 (1950).
- (55) Regna, P. P., Solomons, I. A., Murai, K., Timreck, A. E., Brunings, K. J., and Lauzier, W. A., *J. Am. Chem. Soc.*, **73**, 4211 (1951).
- (56) Robertson, J., Robertson, I., Eiland, P. F., and Pepinsky, R., *J. Am. Chem. Soc.*, **74**, 841 (1952).
- (57) Rose, H. M., *Ann. N.Y. Acad. Sci.*, **53**, 385 (1950).
- (58) Rothstein, E., and Johnson, M., *Am. Rev. Tuberc.*, **69**, 65 (1954).
- (59) Rutter, P. E. H., and Ballantyne, J. C., *Lancet*, **2**, 314 (1952).
- (60) Sayer, R. J., Michel, J. C., Moll, F. C., and Kirby, W. M., *Am. J. Med. Sci.*, **221**, 256 (1951).

- (61) Schoenbach, E. B., Bryer, M. S., and Long, P. H., *Ann. N.Y. Acad. Sci.*, **53**, 245 (1950).
- (62) Segal, M. S., Dulfano, M. J., and Herschfus, J. A., *Quart. Rev. Allergy Appl. Immunol.*, **6**, 399 (1952).
- (63) Smadel, J. E., Jackson, E. B., and Ley, H. L., Jr., *Ann. N.Y. Acad. Sci.*, **53**, 375 (1950).
- (64) Snyder, J. C., Fagen, R., Wells, E. B., Wick, H. C., and Miller, J. C., *Ann. N.Y. Acad. Sci.*, **53**, 362 (1950).
- (65) Steenken, W., Jr., and Wolinsky, E., *Ann. N.Y. Acad. Sci.*, **53**, 399 (1950).
- (66) Weinberg, E. D., *Antibiotics & Chemotherapy*, **4**, 35 (1954).
- (67) Welch, H., *Ann. N.Y. Acad. Sci.*, **53**, 253, (1949).
- (68) Welch, H., Hendricks, F. D., Price, C. W., and Randall, W. A., *J. Am. Pharm. Assoc.*, **39**, 185 (1950).
- (69) Welch, H., and Fobby, G. L., eds., *Medical Encyclopedia*, Medical Encyclopedia, Inc., N.Y., 1954, pp. 233, 262.
- (70) Werner, C. A., Knight, V., and McDermott, W., *Proc. Soc. Exptl. Biol. Med.*, **74**, 261 (1950).
- (70a) Weinberg, E. D., *Bacteriol. Proc.*, **1954**, 80.
- (71) Wong, D. T. O., Barham, S., and Aji, S. J., *Antibiotics & Chemotherapy*, **3**, 607 (1953).
- (72) Wood, W. S., Kipnis, G. P., *Antibiotics Annual*, **1953-54**, p. 98.
- (73) Wright, S. S., Purcell, E. M., Wilcox, C., Broderick, M. K., and Filand, M., *J. Lab. Clin. Med.*, **42**, 877 (1953).
- (74) Wright, W. A., P'an, S. Y., and Carlozzi, M., *Antibiotics Annual*, **1**, 137 (1953).
- (75) Zimmerman, L. E., *U.S. Armed Forces Med. J.*, **3**, 503 (1952).
- (76) Can. Pat. 504,172 (July 6, 1954), E. E. Zimrack, S. W. Ensminger, P. P. Regna, and W. E. Steig (to Chas. Pfizer).
- (77) U.S. Pat. 2,516,080 (July 18, 1950), B. A. Sobin, A. C. Finlay, and J. H. Kane (to Chas. Pfizer).
- (78) U.S. Pat. 2,649,480 (August 18, 1953), A. E. Timreck, P. P. Regna, and R. A. Carboni (to Chas. Pfizer).
- (79) U.S. Pat. 2,658,078 (November 11, 1953), E. W. Blase (to Chas. Pfizer).

PETER P. REGNA

## TETRACYCLINE

Tetracycline (Tetracin, Achromycin, etc.) (26a),  $C_{22}H_{21}N_2O_8$  (formula, p. 772), is the 7-deschloro compound of chlortetracycline and the 5-deoxy compound of oxytetracycline. It is conveniently prepared by catalytic hydrogenation of chlortetracycline (4,5,26) (see p. 777). Tetracycline has also been produced by fermentation of a *Streptomyces* species isolated from a Texas soil sample (19). The antibiotic obtained from this fermentation is identical with the substances obtained by catalytic reduction of chlortetracycline. The antibiotic possesses *in vitro* activity against a wide variety of microorganisms comparable to the broad-spectrum antibiotics oxytetracycline and chlortetracycline. Tetracycline is commercially available as its amphoteric base and as its hydrochloride.

The chemical structure of tetracycline (4-dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro - 3,6,10,12,12a - pentahydroxy - 6 - methyl - 1,11 - dioxo - 2 - naphthacene-carboxamide) was first evident from its mode of formation from chlortetracycline and has been substantiated by degradation studies (2,26).

### Physical and Chemical Properties

Tetracycline is an antibiotic that crystallizes from water-solvent mixtures as a trihydrate. The anhydrous form can be obtained by drying at 60°C. *in vacuo* for several hours; m.p. 170-175°C. (decompn.);  $[\alpha]_D^{25} -239$  (c, 1% in methanol);  $[\alpha]_D^{25} -258$  (0.5% in 0.1 N hydrochloric acid). The trihydrate is soluble in water at 26.5°C, to the extent of 0.36 mg./ml. Crystals of the amphoteric base of tetra-

cycline belong to the orthorhombic system and possess the following refractive indexes:  $\alpha = 1.572 \pm 0.005$ ,  $\beta = 1.646 \pm 0.005$ ,  $\gamma = >1.750$  (19). The ultraviolet absorption spectrum of tetracycline exhibits, in 0.01 *M* methanolic hydrogen chloride,  $\log \epsilon$  4.27 (268  $m\mu$ ),  $\log \epsilon$  4.14 (363  $m\mu$ ); and in 0.01 *M* methanolic sodium hydroxide,  $\log \epsilon$  4.24 (246  $m\mu$ ) and  $\log \epsilon$  4.20 (382  $m\mu$ ) (26).

Tetracycline produces an orange-yellow solution with Ehrlich's reagent (*p*-dimethylaminobenzaldehyde in dilute aqueous hydrochloric acid) and a violet color with sulfuric acid. It exhibits  $pK_a$  values of 8.3, 10.2 (50% aqueous dimethylformamide).

Tetracycline forms salts with acids and bases. For example, the amphoteric base of tetracycline, dissolved in 1-butanol containing hydrochloric acid, crystallizes from this solution as a hydrochloride having the composition  $C_{22}H_{24}N_2O_8 \cdot HCl$ , m.p. 214 (darkens gradually with gaseous evolution (14)). The hydrochloride has a solubility in water of 132 mg./ml. at 26.5°C.

During the preparation of tetracycline (3,5,14,26) from chlortetracycline, one mole of hydrogen is absorbed and one mole of hydrochloric acid is formed. No isomerization takes place during this reaction since the characteristics of the ultraviolet absorption spectra of tetracycline in acidic and basic media are virtually identical with that of oxytetracycline. This inference is deducible from studies of the ultraviolet absorption spectrum of oxytetracycline, which has been shown to involve all four rings of the molecule and is susceptible to change with minor structural alterations (14,26). Further confirmation of the structure of tetracycline has been obtained by dehydration of the antibiotic either by methanolic hydrogen chloride (3,5) or with hydrogen iodide (3) to yield **anhydrotetracycline**, the properties of which are closely related to those of the corresponding anhydro compounds of oxytetracycline (14) (see Scheme 2, p. 793) and chlortetracycline (29). This substance is identical with the reaction product obtained by treatment of chlortetracycline with hydriodic acid (26,29) (see p. 777).

The stability of tetracycline in alkaline solution resembles that of oxytetracycline in contrast to chlortetracycline, which is unstable under such conditions. By using more drastic alkaline conditions, however, tetracycline can be converted to **isotetracycline**, similar in structure to 12a-deoxydesdimethylaminoisooxytetracycline, p. 794. This isomerization is followed by a complex cleavage of the A and B rings in which the dimethylamino group is eliminated with subsequent contraction of ring A to a cyclopentane derivative and the opening of ring B to yield a glutaric acid side chain on the phthalide (3,26). This series of reactions is similar to that shown in Scheme 1 (p. 776) (see also refs. 3, 26) and further confirms the observation that only the replacement of the chlorine atom by a hydrogen atom is involved during the reduction of chlortetracycline to tetracycline.

### Preparation and Manufacture

Hydrogenation of chlortetracycline in the presence of palladized carbon in a dioxane-methanol solution results in the ready hydrogenolysis of the aromatic halogen atom at C-7 to give tetracycline hydrochloride (5). On a more practical scale hydrogenation usually proceeds better in the presence of a base which neutralizes the hydrochloric acid produced in the reaction (4). Consequently, the reduction is carried out by dissolving chlortetracycline in a solvent such as 2-methoxyethanol (methyl Cellosolve), containing a mole of triethylamine, and hydrogenating in the presence of

palladium on charcoal at room temperature. Under these conditions the reaction is somewhat exothermic and is practically complete in about 15-20 minutes after the consumption of one mole of hydrogen.

After removal of the catalyst by filtration, the amphoteric base of tetracycline crystallizes upon dilution of the filtrate with water. The crude material is recrystallized from methanol-water mixture yielding the trihydrate which can be converted to the anhydrous form by drying *in vacuo* at 60° for 8 hours (3). *Tetracycline hydrochloride*,  $C_{22}H_{24}N_2O_8 \cdot HCl$ , can be prepared by dissolving the base in 1-butanol and adding one mole of aqueous hydrochloric acid, whereupon the salt crystallizes readily.

While tetracycline may be produced by fermentation (19), no information has appeared regarding production of the drug by this route. It would appear that fermentation techniques do not as yet compete with chemical methods for the production of tetracycline.

The principal manufacturers of tetracycline are Charles Pfizer & Co., Inc., and Lederle Laboratories, Division of American Cyanamid Co.

**Market Forms.** Tetracycline is available in a variety of dosage forms. Capsules are most widely used for oral administration. However, sugar coated tablets, chocolate-flavored granules, and oral suspensions flavored with cherry, chocolate, and citrus fruit compounds offer more palatable and pleasing therapeutic preparations. In addition, there are available pediatric drops flavored with banana or cherry extracts, a 3% topical ointment, a 1% ophthalmic ointment, an otic preparation, and soluble tablets. An intramuscular dosage form, composed of sterile, pyrogen-free, dry mixtures of crystalline tetracycline hydrochloride, magnesium chloride, procaine hydrochloride, and ascorbic acid, is marketed for patients for whom the oral route is not recommended. For hospitalized patients an intravenous dosage form made up of tetracycline hydrochloride and ascorbic acid is administered.

**Stability.** Tetracycline is very stable in solution at pH 7.0 (2,5). A concentration of 8  $\gamma$ /ml. in physiological saline solution retained its full antibacterial potency for 3 weeks (12). In 0.1 N sulfuric acid it shows no loss of antibiotic activity after 48 hours; however, at pH 8.9 in disodium phosphate the antibiotic loses about 50% of its activity in 12 hours (19). In the frozen state at slightly acid pH, solutions retained full potencies after 6 weeks. Moderate stability of solutions of the antibiotic was noted during 48 hours at 37°C. (34).

### Microbiological Properties

**Antimicrobial Spectra.** Although tetracycline has not been thoroughly evaluated, it is known to possess an activity comparable to the other tetracyclines (9,17,18a). A concentration of less than 1  $\gamma$ /ml. was found to inhibit the growth of *Salmonella typhosa*, *Salmonella paratyphi*, *Brucella bronchiseptica*, *Mycobacterium ranae*, *Streptococcus faecalis* (5), *Klebsiella pneumoniae*, *Streptococcus mitis*, *Pasteurella multocida*, and certain strains of *Staphylococcus aureus* (*Micrococcus pyogenes* var. *aureus*) (9a). It is effective against the lymphogranuloma group viruses (17a). Further work by other investigators (6,9,31,34) has stressed the activity of tetracycline as a broad-spectrum antibiotic.

Eight different genera and twenty-two species or strains of Gram-positive microorganisms, with the exception of two *Corynebacterium* species, were sensitive to tetra-

cycline in a concentration range of 0.312 to 1.56  $\gamma$ /ml. (9,17). Tetracycline was effective in a concentration range of 0.39 to 3.12  $\gamma$ /ml. against nine genera which represented fifteen species of Gram-negative bacteria. The antibiotic showed little activity, if any, against a strain of *Proteus* and only limited activity against a strain of *Pseudomonas aeruginosa* (9) and no effect on *Candida albicans* (9,19). Tetracycline possesses only slight antitoxoplasmic activity in mice infected with toxoplasmosis (10).

No significant differences were noted in the minimum inhibitory concentrations needed for the various microorganisms when the tests were carried out in nutrient broth, brain-heart infusion, veal infusion, and tryptic digest of casein (Trypticase) media. Furthermore, the antibiotic is not inactivated in the presence of human serum, and, like oxytetracycline and chlortetracycline, tetracycline is nonhemolytic for human red blood cells (9).

Tetracycline, like chlortetracycline and oxytetracycline, is primarily bacteriostatic in nature; however, in high concentrations it may act in a bactericidal manner (9,19). *Bacillus subtilis* required only a twofold increase in tetracycline concentration to produce a bactericidal action. With Gram-negative microorganisms in general, a range of four to seventy times was necessary to effect a bactericidal action. In experiments with Gram-positive microorganisms it was noted that two to thirty times the concentration was required (9).

**Development of Resistance.** The increase in resistance to tetracycline by transfer in media containing increasing concentrations of the drug is gained slowly in a gradual, stepwise fashion. This pattern of resistance development is comparable to that of penicillin, chlortetracycline (7), and oxytetracycline (8) and is in contrast to that of streptomycin (9). A strain of *Escherichia coli* did not develop resistance to tetracycline in ten transfers (19). Furthermore, no cross resistance or increases in sensitivity to penicillin, streptomycin, bacitracin, polymyxin, neomycin, or erythromycin developed as a result of the increases in resistance to the tetracyclines (33). However, strains of *Micrococcus pyogenes* var. *aureus* which had been made resistant to either carbomycin or penicillin plus streptomycin by laboratory methods were still sensitive to low concentrations of tetracycline (9).

### Pharmacological Properties

**Absorption and Excretion.** Tetracycline is readily absorbed from the gastrointestinal tract of the rat and the dog and can be found, for example, in the urine of rats within 2 hours after an oral administration of 10 mg./kg. Single intravenous injections of 10 mg. of tetracycline per kilogram produced appreciable blood levels in the dog for at least 24 hours. The antibiotic is concentrated in the bile of these animals following intravenous injection and, moreover, can be found in the cerebrospinal fluid (6). The intravenous administration of tetracycline in the rabbit affords significant serum concentrations. The highest serum levels, 294  $\gamma$ /ml., are observed in the first hour after administration.

Pharmacologic studies in normal subjects after ingestion of a single dose of 1 g. of tetracycline showed rapid and high concentrations of the antibiotic in the blood stream and in the urine. Blood concentrations following various oral doses of tetracycline compared well with similar doses of chlortetracycline (22,28,32,34).

The antibiotic is absorbed from the gastrointestinal tract after oral administration and subsequently appears in the various body fluids, including blood serum, spinal

fluid, abdominal fluid, chest fluid, saliva, cord serum, and urine. A large portion of the ingested dose that is not absorbed from the gastrointestinal tract is recovered in the stool.

After intravenous administration, the antibiotic diffuses from the blood into various body fluids. It is also present in small amounts in the feces (18). Higher serum and cerebrospinal fluid concentrations were found with tetracycline (32) than with the other tetracyclines. Young male patients treated with 500 mg. of tetracycline by the intravenous route showed after 1 hour 0.45  $\gamma$ /g. in the prostate and 3.9  $\gamma$ /g. in the semen when the average blood level was 7.0  $\gamma$ /g. (1).

**Toxicity.** Tetracycline was found to have a low order of toxicity comparable to that of oxytetracycline and chlortetracycline when its pharmacological properties were studied in mice, rats, rabbits, and dogs (6,9,19). The oral LD<sub>50</sub> was found to be greater than 3,000 mg./kg. in mice and rats. Moreover, single daily oral doses of 100 mg./kg. to mice, 5 days per week for 6 weeks, produced no significant changes in any elements of the complete blood count. The animals grew at an accelerated rate. The intravenous LD<sub>50</sub> in mice was 170 mg./kg., and in rats 220 mg./kg. Daily intravenous injections in dogs for relatively long periods produced no deviation from normal in liver or kidney function tests, blood-clotting time, nonprotein nitrogen levels, blood-sugar levels, and complete blood counts. In this careful pharmacological evaluation, tetracycline was found to have no significant anticoagulant, antispasmodic, anticonvulsant, cardiovascular, or respiratory effects (6). The intraperitoneal LD<sub>50</sub> was 330 mg./kg. in mice and 320 mg./kg. in rats.

In human patients tetracycline was found to be tolerated at high levels (19,22,34). Doses of tetracycline of 1 g. every 6 hours were well tolerated, even when these doses were not given in relation to meals or supplementary feedings (19,34). Untoward gastrointestinal symptoms, particularly diarrhea, did not occur with a single dose of 1 g. of the antibiotic (21).

Preliminary studies with tetracycline have shown a minimum number of side reactions. In a study of 217 healthy male subjects, only 4 exhibited what may have been an allergic response to the drug. Nausea, vomiting, and diarrhea occurred in only 5.5% of these subjects on a dosage schedule of 2 g. tetracycline daily for 3 days (19,34). In one study 18% of patients exhibited loose stools, but only a small percentage of the group showed any intestinal disturbances (22,27,34). Some 50–60% of these 217 subjects showed no evidence of reactions at all from the drug (18,22). There appear to be even less toxic effects from intravenous infusions (34).

Patients treated with tetracycline show clinical responses accompanied by some mild gastrointestinal side effects (28), transient nausea and vomiting, slight looseness of stool, and some indisposition in certain individuals due to a metallic taste (35).

Infrequent gastrointestinal tract disorders can be diminished if the drug is taken with milk immediately after meals or with antacids. Aluminum hydroxide gels given with antibiotics, however, have been shown to decrease absorption and are contraindicated (20).

Because tetracycline, when administered orally, suppresses growth of bacteria in the intestine, its use may occasionally result in an overgrowth of nonsusceptible organisms, such as monilia. Therefore, it may be advisable to administer a vitamin B complex supplement to patients receiving tetracycline orally for prolonged periods of time. Surveillance of the patient is suggested in order to detect a superimposed infection, certain individual idiosyncrasies, allergic reactions, glossitis, and dermatitis.

**Administration and Dosage.** The dosage of tetracycline required to produce optimum therapeutic response will vary, from one patient to another, with the severity, response, and susceptibility of the infection. The same dosages of tetracycline base (anhydrous and hydrated forms) or its hydrochloride are equally effective. In the average adult the suggested minimum daily dose is 1-2 g. divided into four equal parts (34), and for children proportionately less, for example 50 mg. four or five times daily. Duration of therapy is recommended for at least 24-48 hours after symptoms and fever have subsided. Certain diseases are treated in courses, such as a 10- to 14-day period in acute staphylococcal infections or brucellosis. In such cases as subacute bacterial endocarditis, therapy for 6-8 weeks is recommended.

### Specifications and Assay

The manufacturers of tetracycline maintain rigid requirements for the purity of the antibiotic, and the drug must pass Food and Drug Administration specifications (published in the *Federal Register*) as well. Its identity is established by several colorimetric tests (as, for example, the appearance of a purple color with sulfuric acid with subsequent change to an orange-yellow color on addition of water) and by determination of its optical rotation and its absorption maxima in 0.01 *N* hydrochloric acid between 290 and 315 at 353 m $\mu$ . Acid hydrolyzates of tetracycline are estimated spectrophotometrically by comparison with a standard at 430 m $\mu$ . In addition, a series of purity tests is recommended which include infrared spectrum, estimation of heavy metals, loss of weight on drying, residue on ignition, pH of a solution, solubility in water and ethyl alcohol, and general physical appearance. Parenteral products must be sterile (absence of bacteria, molds, yeasts, etc.); nontoxic; nonpyrogenic; and free of any depressor substances such as histamine.

The microbiological assays are carried out by a turbidimetric method (15) using *Klebsiella pneumoniae* (A.A.T.C. 10031, P.C.I. 602) and an incubation period of 3.5 hours with crystalline anhydrous tetracycline as a standard. The procedure has been applied successfully to both impure and purified preparations of tetracycline. Satisfactory test results have been obtained also with agar streak, agar diffusion and modified turbidimetric methods (2). In addition, moderately reliable methods for determination of tetracycline in biological fluids have been devised using various test microorganisms (9,12,19,32,34).

### Uses and Indications

Although tetracycline has not been fully evaluated clinically, it has been found effective in a variety of microbial infections (30a), including pneumonia, surgical infections, urinary tract infections (9,12,13,16,27,35), conjunctivitis, diarrhea, gangrenous appendicitis (16), soft tissue infections (18), meningococcal meningitis (12), several bronchopulmonary infections with acute exacerbations (12), cholangitis (35), and exanthematic (classical) typhus (24). Acute hemolytic streptococcal pharyngitis has shown excellent bacteriological and clinical responses (33). An increase in the inhibition of certain strains of *Endamoeba histolytica* was observed when tetracycline was combined with oxytetracycline (25).

The antibiotic has been used also with good clinical results in some cases of acute bronchitis, mixed bacterial infections, scarlet fever, osteomyelitis, epidermal abscesses, acute brucellosis, pancreatic fibrosis, sinusitis, and gonorrhea, and in bacterial



endocarditis produced by both Gram-positive and Gram-negative bacteria sensitive to tetracycline (30).

### Bibliography

- (1) Borski, A. A., Pulaski, E. J., Kimbrough, J. C., and Fusillo, M. H., *Antibiotics & Chemotherapy*, **4**, 905 (1954).
- (2) Bohonos, N., Dornbush, A. C., Feldman, L. I., Martin, J. H., Pelcak, E., and Williams, J. H., *Antibiotics Ann.*, **1953-54**, p. 49.
- (3) Boothe, J. H., Morton, J., II, Petisi, J. P., Wilkinson, R. G., and Williams, J. H., *Antibiotics Ann.*, **1953-54**, p. 46.
- (4) Boothe, J. H., Morton, J., II, Petisi, J. P., Wilkinson, R. G., and Williams, J. H., *J. Am. Chem. Soc.*, **75**, 4621 (1953).
- (5) Conover, L. H., Moreland, W. T., English, A. R., Stephens, C. R., and Pilgrim, F. J., *J. Am. Chem. Soc.*, **75**, 4622 (1953).
- (6) Cunningham, R. W., Hines, L. R., Stokey, E. H., Vessey, R. E., and Yuda, N. N., *Antibiotics Ann.*, **1953-54**, p. 63.
- (7) Demerco, M., *J. Clin. Invest.*, **28**, 891 (1949).
- (8) English, A. R., and Gelwicks, P. C., *Antibiotics & Chemotherapy*, **1**, 118 (1951).
- (9) English, A. R., Pan, S. Y., McBride, T. J., Gardocki, J. F., Van Halsema, G., and Wright, W. A., *Antibiotics & Chemotherapy*, **4**, 411 (1954).
- (9a) English, A. B., McBride, T. J., Simon, D. L., and Mullady, H. E., *Antibiotics & Chemotherapy*, **4**, 1082 (1954).
- (10) Eyles, D. E., and Coleman, N., *Antibiotics & Chemotherapy*, **4**, 988 (1954).
- (11) Farber, J. E., Ross, J., and Stephens, G., *Calif. Med.*, **9**, 81 (1954).
- (12) Finland, M., Purcell, E. M., Wright, S. S., Love, B. D., Jr., Mou, T. W., and Kass, E. H., *J. Am. Med. Assoc.*, **154**, 561 (1954).
- (13) Glatt, M., and Ross, S., *Antibiotics & Chemotherapy*, **4**, 395 (1954).
- (14) Hochstein, F. A., Stephens, C. R., Conover, L. H., Regna, P. P., Pasternack, R., Gordon, P. N., Pilgrim, F. J., Brunings, K. J., and Woodward, R. B., *J. Am. Chem. Soc.*, **75**, 5455 (1953).
- (15) Kersey, R. C., *J. Am. Pharm. Assoc., Sci. Ed.*, **39**, 252 (1950).
- (16) Lawlor, E. G., Cella, P. J., and DeVera, J., *Clin. Med.*, **61**, 207 (1954).
- (17) Love, B. D., Jr., Wright, S. S., Purcell, E. M., Mou, T. W., and Finland, M., *Proc. Soc. Exptl. Biol. Med.*, **85**, 25 (1954).
- (17a) Marmell, M., and Prigot, A., *Antibiotics & Chemotherapy*, **4**, 1117 (1954).
- (18) Maynard, A. L., Andriola, J. C., and Prigot, A., *Antibiotics Ann.*, **1953-54**, p. 102.
- (18a) Milberg, M. B., Kamhi, B., and Banowitch, M. M., *Antibiotics & Chemotherapy*, **4**, 1086 (1954).
- (19) Minieri, P. P., Firman, M. C., Mistretta, A. G., Abbey, A., Bricker, C. E., Rigler, N. E., and Sokol, H., *Antibiotics Ann.*, **1953-54**, p. 81.
- (20) Paul, H. E., and Harrington, C. M., *J. Am. Pharm. Assoc., Sci. Ed.*, **41**, 50 (1952).
- (21) Purcell, E. M., Wright, S. S., Mou, T. W., and Finland, M., *Proc. Soc. Exptl. Biol. Med.*, **85**, 61 (1954).
- (22) Putnam, L. E., Hendricks, F. D., and Welch, H., *Antibiotics & Chemotherapy*, **3**, 1183 (1953).
- (23) Regna, P. P., *Trans. N.Y. Acad. Sci.*, **15**, 12 (1952).
- (24) Sánchez, F. R., Sánchez, A. R., Becerra, A., and Granada, E. N., *Antibiotics & Chemotherapy*, **4**, 402 (1954).
- (25) Seneca, H., and Bergendahl, E., *Am. J. Med. Sci.*, **228**, 16 (1954).
- (26) Stephens, C. R., Conover, L. H., Hochstein, F. A., Moreland, W. T., Regna, P. P., Pilgrim, F. J., Brunings, K. J., and Woodward, R. B., *J. Am. Chem. Soc.*, **76**, 3568 (1954).
- (26a) Stephens, C. R., Conover, L. H., Hochstein, F. A., Regna, P. P., Pilgrim, F. J., Brunings, K. J., and Woodward, R. B., *J. Am. Chem. Soc.*, **74**, 4976 (1952).
- (27) Trafton, H. M., and Lind, H. E., *Antibiotics & Chemotherapy*, **4**, 697 (1954).
- (28) Waddington, W. S., Bergy, G. G., Nielsen, R. L., and Kirby, W. M. M., *Am. J. Med. Sci.*, **228**, 164 (1954).
- (29) Waller, C. W., Hutchings, B. L., Broschard, R. W., Goldman, A. A., Stein, W. J., Wolf, C. F., and Williams, J. H., *J. Am. Chem. Soc.*, **74**, 4981 (1952).
- (30) Welch, H., *Antibiotics & Chemotherapy*, **4**, 375 (1954).

- (30a) Welch, H., *Principles and Practice of Antibiotic Therapy*, Medical Encyclopedia, Inc., N.Y., 1954, ch. XI.
- (31) Welch, H., Randall, W. A., Reedy, R. J., and Oswald, E. J., *Antibiotics & Chemotherapy*, **4**, 741 (1954).
- (32) Wood, W. S., and Kipnis, G. P., *Antibiotics Ann.*, **1953-54**, p. 98.
- (33) Wright, S. S., and Finland, M., *Proc. Soc. Exptl. Biol. Med.*, **85**, 40 (1954).
- (34) Wright, S. S., Purcell, E. M., Love, B. D., Jr., Mou, T. W., Kass, E. H., and Finland, M., *Antibiotics Ann.*, **1953-54**, p. 92.
- (35) Young, W. B., and Tuttle, J. G., *Am. J. Med.*, **16**, 612 (1954).

PETER P. REGNA

**1-TETRADECANOL**,  $\text{CH}_3(\text{CH}_2)_{12}\text{CH}_2\text{OH}$ ; **"TETRADECANOL,"**  $\text{CH}_3(\text{CH}_2)_3\text{-CH}(\text{C}_2\text{H}_5)\text{CH}_2\text{CH}_2\text{CHOHCH}_2\text{CH}(\text{CH}_3)_2$ . See *Alcohols, higher*, Vol. **1**, p. 319.

**TETRAETHYLAMMONIUM ION**,  $(\text{C}_2\text{H}_5)_4\text{N}^+$ . See *Stimulants and depressants*, p. 35.

**TETRAETHYL LEAD**,  $(\text{C}_2\text{H}_5)_4\text{Pb}$ . See *Lead compounds (tetraethyl lead)*, Vol. **8**, p. 274; *Organometallic compounds*, Vol. **9**, p. 635.

**d-TETRAHYDROCOPTISINE**,  $\text{C}_{19}\text{H}_{17}\text{NO}_4$ . See *Alkaloids*, Vol. **1**, p. 486.

**d-TETRAHYDROPALMATINE**,  $\text{C}_{21}\text{H}_{25}\text{NO}_4$ . See *Alkaloids*, Vol. **1**, p. 486.

**TETRANTROMETHANE**,  $\text{C}(\text{NO}_2)_4$ . See *Explosives (high)*, Vol. **6**, p. 22; *Rocket propellants*, Vol. **11**, p. 772.

**TETRATRIACONTANOIC ACID**,  $\text{C}_{38}\text{H}_{76}\text{COOH}$ . See *Fatty acids*, Vol. **6**, pp. 174, 259.

**TETRAZOLES**,  $\text{CH:N:N:N:NH}$ . See *Heterocyclic compounds*, Vol. **7**, p. 445.

**TETRITOLS**. See *Alcohols, higher polyhydric*, Vol. **1**, p. 322.

**TETROLIC ACID**,  $\text{CH}_3\text{C:CCOOH}$ . See *Fatty acids (survey)*, Vol. **6**, p. 177.

**TETRYL**,  $\text{CH}_3\text{N}(\text{NO}_2)\text{C}_6\text{H}_2(\text{NO}_2)_3$ . See *Explosives (high)*, Vol. **6**, p. 51.

**TETRYTOL**. See *Explosives (high)*, Vol. **6**, p. 57.

**TEXONIN; TEXOGENIN**,  $\text{C}_{22}\text{H}_{33}\text{O}_4$ . See *Saponins and sapogenins*, Vol. **12**, p. 100.

## TEXTILE FIBERS, SYNTHETIC

Survey.....	810	<b>Tetrafluoroethylene Fibers</b> .....	847
Acrylic and Other Vinyl Fibers.....	824	<b>Glass Fibers</b> .....	849
Polyester Fibers.....	840		

See also *Polyamides; Protein fibers, synthetic; Rayon and acetate fibers*.

## SURVEY

Food, clothing, and shelter are the three primary requirements of mankind, and from the earliest time man has continually striven to improve the quality and availability of these basic items. For this reason, few developments in recent years have affected the average person so profoundly as the growing field of synthetic fibers. Bringing the quality associated with the luxury fibers in the past within the reach of everyone, they have made available finer and more durable garments for all.

The principal domestic semisynthetic and synthetic fibers and their producing companies are listed in Table I. The year of introduction to the textile trade in the

U.S., noted in Table I, is often difficult to determine, as the announcement of the fiber, pilot plant, and semicommercial production, and selection of a trade name are often spread over a period of several years.

TABLE I. Principal Domestic Synthetic Fibers and Producing Companies.

Chemical class	Fiber	Producing companies
Cellulose	Viscose rayon (1911)	American Enka Corp.; American Viscose Corp.; Beaunit Mills; Celanese Corp. of America; Courtaulds (Alabama) Inc.; Delaware Rayon Co.; E. I. du Pont de Nemours & Co.; Fair Haven Mills, Inc.; Hartford Rayon Co.; North American Rayon Corp.; Industrial Rayon Corp.; New Bedford Rayon Co.; Skenandoa Rayon Corp.
	Cuprammonium rayon (1925)	Beaunit Mills, Inc., American Bemberg Div.
	Fortisan (1941)	Celanese Corp. of America; E. I. du Pont de Nemours & Co.
Cellulose acetate	Acetate (1924)	American Viscose Corp.; Celanese Corp. of America; E. I. du Pont de Nemours & Co.; Tennessee Eastman Corp.
Protein	Vicara <sup>a</sup> (1948)	Virginia-Carolina Chemical Corp.
Polyamide	Nylon (1938)	Chemstrand Corp.; E. I. du Pont de Nemours & Co.
Vinyl	Vinyon HH <sup>a</sup> (1939)	American Viscose Corp.
	Saran (1940-47)	Bolta-Saran, Inc.; Dawbarn Bros., Inc.; Firestone Plastics Co.; Lus-Trus Extruded Plastics, Inc.; National Plastics Products Co.; Oriented Plastics; Saran Yarns Co.
	Polyethylene (1947)	Firestone Plastics Co.; National Plastics Products, Inc.; Reeves Bros., Inc.
Vinyl-acrylic	Dynel (1950)	Carbide & Carbon Chemicals Co.
Acrylic	Orlon <sup>a</sup> (1948-50)	E. I. du Pont de Nemours & Co.
	Acrilan <sup>a</sup> (1950-52)	Chemstrand Corp.
Polyester	Daeron <sup>a</sup> (1950)	E. I. du Pont de Nemours & Co.
Inorganic	Glass (1930)	Ferro Corp.; Glass Fibers, Inc.; Libbey-Owens-Ford Glass Co.; Owens-Corning Fiberglas Corp.; Pittsburgh Plate Glass Co.; U.S. Glass Fiber Co.

<sup>a</sup> Trade-mark registered in U.S. Patent Office.

**Semisynthetic Fibers.** In 1883 Weston produced experimental filaments from an ether-alcohol solution of nitrocellulose, and shortly thereafter Swan found that the product could be denitrified with ammonium sulfide, thus regenerating the cellulose. Count Chardonnet then developed a procedure for pumping Weston's solution through minute orifices into a chimney through which warm air was circulated to remove the solvent, after which the filaments were treated with ammonium sulfide. This led to the construction of the first plant for the production of rayon at Besançon, France, in 1891.

The Chardonnet process was essentially a dry-spinning operation. Other methods for the production of cellulosic fibers were soon developed, the majority of which employed wet-spinning procedures. In the viscose process, developed by Cross and

Bevan, a cellulose xanthate solution is extruded into a liquid bath which simultaneously precipitates and regenerates the cellulose. In the cuprammonium process developed by Fremery, Urban, and Despaissis, a solution of cellulose in ammoniacal copper hydroxide is spun into a liquid bath which coagulates the fibers and regenerates the cellulose.

In addition to regenerated cellulose fibers, chemically modified cellulose fibers were developed. Cellulose was acetylated, dissolved in acetone, and spun into warm air to form acetate fibers.

Sold under the name of artificial silk, these semisynthetic fibers were an instant success. Although some of the rayon and acetate initially placed on the market was undeniably poor in quality, constant research improved the quality and appearance of these fibers to their present high level.

It was inevitable that certain processes would be found to be more efficient than others in the production of fibers. The nitrate process was soon abandoned, while the cuprammonium process was found to have only limited application. The bulk of the cellulosic fiber produced today is manufactured by the viscose process.

It is significant that the first of the man-made fibers to be produced commercially was derived from a natural polymer, cellulose. Acetate, although it does not consist chemically of unmodified cellulose, is based on the natural cellulose polymer structure.

The early work on synthetic fibers was carried out almost entirely in Europe. This was due to the fact that England, France, and Germany had well-established chemical industries and could supply the technical knowledge required for developing the complex operations used in the production of cellulosic fibers. Shortly after the turn of the century, the infant chemical industry in the U.S. started to expand, to be followed shortly by the manufacture of rayon. The first plant was constructed at Marcus Hook in 1911 and was operated by the American Viscose Corp. until 1954. Military demands during World War I resulted in a very rapid growth in the American chemical industry, and, with this as a base, the production of rayon was carried out on an ever-expanding scale. Rayon accounted for approximately 5% of the textile fibers sold in the U.S. by 1930, and by 1938 it passed wool and was second only to cotton in terms of annual consumption. The first successful acetate plant was operated by the Celanese Corp. at Cumberland, Md., in 1924. The initial production was quite small, but by the middle of the century it amounted to one-third of the total domestic cellulosic fiber production.

The efforts of the early investigators in the cellulosic fiber field were directed toward the development of continuous silklike filaments and yarns. During the first three or four decades of the rayon industry, its output was almost exclusively confined to continuous multifilament yarns which could be used in place of silk for the construction of fine fabrics and garments. Early acetate production also was confined to the production of continuous filament yarns.

As a better understanding of the properties of rayon and acetate was attained, it was evident that each was an entirely new fiber and that broader fields of application could be developed by taking advantage of the unique properties of each fiber. Since an overwhelming majority of the natural fibers in use were in staple form, and since well-developed procedures were available for converting staple fibers into yarn, the production of staple from rayon and acetate was initiated.

By cutting the rayon and acetate tows obtained from the spinning process into various lengths, staple fiber suitable for use in the cotton, woolen, and worsted systems

could be produced at will. As the staple length could be controlled within very narrow limits, which is not possible with natural fibers, the synthetic staple could be converted into yarn which upon weaving or knitting gave fabrics having properties unobtainable with natural fibers. In addition to cutting into uniform lengths, methods also were developed that made it possible to cut synthetic fibers into random lengths to simulate the staple pattern of natural fibers.

The production of staple instead of continuous filament yarns permitted a substantial reduction in production costs due to the larger number of filaments which could be spun in staple operations. While 300 filaments per spinneret are usually regarded as the upper limit in continuous filament yarn production, as many as 20,000 filaments can be obtained from one spinneret in the production of staple.

The mechanical, thermal, and surface characteristics of yarns spun from staple are quite different from those of continuous filament yarns, and therefore the provision of synthetic fibers in staple form made possible a great increase in the number of fabrics available for the apparel and other trades. Another factor stimulating development was the possibility of blending both natural and artificial staples in any desired proportion. As certain of the properties of the natural and synthetic fibers complemented each other, judicious blending led to the development of fabrics having outstanding service and appearance characteristics.

The impact of these developments upon the domestic cellulosic fiber industry is reflected in the production pattern for the industry. Shortly after the development of the staple-cutting process in the middle 1930's, only 1% of the total rayon and acetate production was being sold in the form of staple. During the next 15 years, this proportion was increased at a more or less constant rate to 25%.

While staple rayon was becoming an established factor in the industry, further work led to the development of high-tenacity rayon. This found its greatest field of utilization in tire cords, a field heretofore reserved almost exclusively for cotton. Tire cords represented the largest industrial application for cotton, approximately 750,000 bales being consumed annually for this purpose. High-tenacity rayon amounted to only 0.3% of the domestic rayon production in 1937, but by 1950 this had increased to 25%. At the present time over 90% of the tire cord used in the U.S. is fabricated from high-tenacity rayon.

These two developments, namely, staple and high-tenacity rayon, were largely responsible for the phenomenal growth of the rayon and acetate industry illustrated in Table II.

TABLE II. Rayon and Acetate Production.  
(In Million Pounds)

Year	U.S. production			World production		
	Filament	Staple	Total	Filament	Staple	Total
1910	—	—	—	18	—	18
1920	10	—	10	33	—	33
1930	127	$\frac{1}{2}$	127 $\frac{1}{2}$	451	6	457
1940	390	81	471	1181	1282	2463
1950	954	305	1259	1929	1565	3494
1952	829	307	1136	1835	1750	3585
1953	887	310	1197	2040	2050	4090

The 1953 domestic production of cellulosic fibers was divided between 876 million pounds of rayon and 321 million pounds of acetate.

**Synthetic Fibers.** In 1927 the Du Pont Co. inaugurated a fundamental research program which was to result in the first true synthetic fiber to achieve commercial importance, nylon. The development of fully synthetic (or chemical) fibers not only broadened the base of the man-made fiber industry by making available to it the resources of the chemical industry, but also permitted the formation of polymers having properties decidedly different from those of the naturally occurring cellulose and protein polymers.

Nylon, the result of this work, is a polyamide fiber. The polymer is produced by the reaction of adipic acid and hexamethylenediamine, followed by polymerization to the desired molecular weight. The polymer is melted, forced through minute openings in a spinneret, and solidified in a chimney to form filaments by a blast of cold air or gas. Only synthetic fibers can be spun by the melt process, as the natural polymers used in the production of fibers do not possess definite softening or melting points. However, not all synthetic fibers are spun by this process. Some do not have definite softening or melting points and, hence, must be spun by either dry- or wet-spinning procedures, which are also used in certain other cases for advantageous fiber properties or economies of operation.

The first nylon spinning plant was located at Seaford, Del. Additional plants were constructed later by Du Pont at Martinsville, Va., and Chattanooga, Tenn.

Probably no major product has ever timed its entry into the industrial field as well as nylon. Placed on the market in 1938, and possessing many of the properties of silk, it was immediately pressed into military use as soon as the supplies of this natural fiber were cut off as a result of the war with Japan. Without nylon for the fabrication of parachutes, glider tow ropes, and a thousand and one other military items, the war effort would have been severely handicapped.

In the apparel field it soon began to challenge silk for the construction of ladies' hosiery. In this use it was found to outlast silk several times over, and the word itself became synonymous with ladies' hose. Quickly expanding its field of utilization to the manufacture of other fine fabrics and garments at the end of the war, it has come to be regarded by many textile experts as the outstanding fiber among all natural and synthetic fibers.

Despite the efforts of Du Pont to keep production and consumption in balance, nylon continued to be in short supply, and many fields of application were neglected because of the impossibility of diverting any of the product from established outlets. To assist in meeting this pent-up demand, Chemstrand Corp. has constructed and is now operating a nylon plant at Pensacola, Fla.

Another polyamide fiber, nylon 6 (see Vol. 10, p. 917) was developed largely in Germany as Perlon during and after World War II. The polymer is obtained from caprolactam, and it is usually converted to fibers by the melt-spinning process. Du Pont also has investigated the production of this fiber on a limited commercial scale. The Allied Chemical and Dye Corp., the American Enka Corp., the A. L. Erlanger Co., and the Industrial Rayon Corp. are constructing plants for the manufacture of nylon 6 at the present time.

Nylon also is manufactured in England, France, Switzerland, and Italy. It is produced and sold under the trade names Amilan and Niplon in Japan.

While the entry of Chemstrand into the nylon production picture, as well as the

entry of several other producers into the nylon 6 field, undoubtedly will help to meet the continuing demands for nylon, a new development now under way could change this situation profoundly. This is the rapidly growing use of nylon in tire cord and fabric.

Owing to the great strength and resiliency of nylon, as well as its resistance to degradation by moisture, it is an almost ideal material for this purpose. Good results have been obtained on a limited commercial production basis, and it is expected that nylon cords will be used extensively in airplane tires, heavy-duty tires, and truck tires. Its use in passenger tires on a large scale also is a distinct possibility.

If quality and economic factors are sufficiently promising, it is conceivable that the tire industry might convert from rayon to nylon cords as rapidly as it converted from cotton to rayon cords a decade ago. Such a conversion would require substantially the entire production of nylon in the U.S. at present production rates, but there is little possibility that it will occur so abruptly or in such a large volume. To meet the challenge offered by nylon cords, the rayon producers have developed a series of super high-tenacity yarns (see Vol. 11, p. 545) which are meeting a favorable reception in the industry. The conversion from rayon to nylon probably will take place gradually, and rayon probably will retain a substantial portion of the market.

Encouraged by the warm reception accorded nylon, the textile industry demanded additional new fibers having a whole spectrum of unusual properties to enable new fabrics and styles to be developed for the retail trade. As not all the properties required were available in natural fibers, or in the synthetic fibers already on the market, large research and development programs were initiated by chemical and fiber companies to meet these demands.

This has resulted in the development and commercial production of several new fibers, such as Acrilan, Dacron, Orlon, and Dynel. With the broad range of properties available in these new fibers, and the almost infinite varieties that can be created by skillful blending with natural fibers and the established semisynthetic and synthetic fibers, the textile industry is preparing fabrics and other consumer items in which new styling, comfort, and durability standards are being attained. The chief consumer appeal of these new synthetics is that they will bring the quality associated with the luxury fibers in the past within the reach of everyone.

The *acrylic fibers* were produced on an experimental basis both in Germany and in the U.S. during World War II. The development of this fiber is another example of the profound effect of chemical developments upon fiber technology. Polyacrylonitrile had been known for almost a generation, but it could not be melted and was insoluble in all known solvents. It was first dissolved in aqueous solutions of inorganic salts and acids, but initial efforts to produce satisfactory fibers from such solutions were unsuccessful. With a development of a better understanding of the mechanism of solvent action, organic compounds that would dissolve polyacrylonitrile to form satisfactory spinning dopes were discovered. This led to the development of both wet- and dry-spinning procedures for the manufacture of acrylic fibers.

These fibers are manufactured on a substantial scale only in the U.S., although several acrylic fibers, such as Redon, Pan, and Dolan, are being produced on an experimental or small-scale basis in Germany. The principal acrylic fibers in the U.S. are Acrilan, produced by Chemstrand, and Orlon, Du Pont's acrylic fiber. These fibers are derived from polyacrylonitrile, or from polyacrylonitrile copolymers containing minor proportions of other ingredients. Dynel, a vinyl-acrylic fiber, is manu-

factured by Carbide & Carbon Chemicals Co. Several experimental acrylic fibers, such as American Cyanamid's X-51 and X-54, also are in various stages of development in the U.S. and abroad.

Acrilan acrylic fiber is produced in staple form by Chemstrand at Decatur, Ala., while both staple and continuous filament Orlon acrylic fiber are produced by Du Pont at Camden, S.C. Dynel is produced in staple form by Carbide & Carbon at Charleston, W.Va.

The initial work on the production of *polyester fibers* was carried out on laboratory scale by Du Pont in the 1930's although the actual development of this fiber on a successful commercial scale was accomplished by Whinfield and his associates in England during World War II. It was first manufactured in England under the trade name Terylene, and Du Pont later obtained the American rights for the process and developed a similar fiber, known as Dacron.

Dacron polymer is produced by the reaction of terephthalic acid, usually in the form of its methyl ester, and ethylene glycol. The polymer is converted to fibers by the melt-spinning process. The Du Pont plant for the production of Dacron continuous filament yarns and staple is located at Kinston, N.C.

**Other Semisynthetic and Synthetic Fibers.** In addition to the fibers listed, other semisynthetic and synthetic fibers have been produced in the U.S. and abroad. While certain of these fibers are of substantial commercial importance, others have been produced in only limited quantities. Lanusa, a wool-like regenerated cellulose staple, is manufactured by the Badische Anilin und Soda Fabrik at Leverkusen, Germany. Tenaseo, Durafil, and Fortisan are highly oriented regenerated cellulose yarns. The first two listed are produced by Courtaulds, Ltd., in Great Britain, and the last is produced in the U.S. and in Great Britain. Fiber E is a viscose rayon yarn which has the property of crimping when treated with a dilute solution of caustic soda. It is manufactured by Du Pont.

A number of *alginate fibers* have been prepared from alginic acid derived from seaweed. All are soluble in water or dilute alkaline solutions, and calcium alginate fibers are used in applications in which a soluble fiber or yarn is required. Large-scale use of alginic fibers awaits the development of a fiber that is insoluble in mild alkaline solutions. Chromium alginate fibers were used in England during World War II for camouflage purposes. At present only calcium alginate fibers are being produced on a commercial scale. These fibers are used in the production of very fine fabrics by blending with wool or any other suitable fiber, weaving, and washing out the alginic fiber from the resulting fabric. Alginic fibers also are used as separators in continuous sock-knitting processes, in the production of fabrics from twistless yarn, in the preparation of astrakhan fabrics, in the manufacture of intermittent lengths of yarn, in embroidery manufacture, and in the fulling of rabbit wool.

A number of fibers also have been prepared from *casein*. The large-scale production of Lanital from casein was started in Italy in 1937, to be followed by the production of Aralac from the same raw material by Aralac, Inc., in the U.S. in 1943. The production of Aralac was discontinued in 1948. Fibrolane A and Fibrolane BX are manufactured by Courtaulds, Ltd., in England from casein. Merinova is a new casein fiber made by Snia Viscosa at Milan, Italy. Caslen, a casein-base fiber, is produced in the U.S. by the Rubberset Co. The outstanding properties of casein fibers are warmth and softness, while their main defect is the substantial loss in strength when wet. This has largely limited their use.



Ardil is a *vegetable protein fiber* manufactured from peanut protein by Imperial Chemical Industries, Ltd., in England. A corresponding fiber, Fibrolane C, is produced by Courtaulds, Ltd., in the same country.

A substantial amount of work also has been carried out on the preparation of fibers from *soybean proteins* in Japan, England, and the U.S. The first fibers were spun in the U.S. in 1939 by Ford Motor Co. The process was taken over by the Dracket Products Co. in 1943, and the product sold under the trade name Azlon.

Vicara is the best of the regenerated protein fibers that has yet been produced. It is prepared from *corn zein* by the Virginia-Carolina Chemical Corp. It has a warm, soft hand and blends readily with wool. Only two other protein fibers, Ardil and Merinova, are being manufactured as of 1954.

Celanese Corporation of America introduced Arnel in October, 1954. This is a fiber spun from a cellulose triacetate, that is, it is more highly acetylated than regular acetate fiber. It can be ironed at comparatively high temperatures and has quick drying characteristics, durable crease retention, and other favorable properties.

In the field of synthetic fibers three different Perlon fibers were made in Germany during World War II. Perlon T is a copy of the Du Pont nylon 66 fiber, prepared from adipic acid and hexamethylenediamine. Perlon L (or nylon 6) is prepared from caprolactam. Perlon L is known as Phrilon in Germany, as Enkeslon in Holland, as Grilon in Switzerland, and as Kapron in Russia. Perlon U is made from hexamethylene diisocyanate and tetramethylene glycol. Only Perlon L appears to offer much promise in the textile field in the future.

The first experimental *vinyl fibers* were prepared by Carbide & Carbon Chemicals Co., but the first commercial production was accomplished in 1936 by American Viscose Corp., using a vinyl chloride-vinyl acetate copolymer supplied by the former company. It is interesting to note that this actually antedated the first commercial production of nylon. The fiber was sold under the trade name Vinyon. Vinyon E was an elastic vinyon first marketed in 1942. Vinyon HH, a staple fiber, is manufactured by American Viscose Corp. It is sold in two forms, UST Vinyon HH and MST Vinyon HH. Vinyon N, a vinyl chloride-acrylonitrile copolymer, was manufactured by Carbide & Carbon Chemicals Co.

A polyvinyl acetate fiber, Avisco Vinyon, is produced by American Viscose Corp., while a polyvinyl chloride fiber, 45, is manufactured by Polymer, Inc.

Saran, a vinylidene chloride-vinyl chloride copolymer, produced by Dow Chemical Co., is spun into a fiber, referred to generically as saran fiber, by a number of companies and sold under the trade names Velon, Boltaflex, Dawbarn, Lus-Trus, National, and Oriented. In England it is spun by BX Plastics and sold under the trade name Tygan.

A number of other vinyl fibers also have been produced abroad. PeCe, a chlorinated polyvinyl chloride fiber, was developed in Germany during World War II. PCU is a polyvinyl chloride fiber developed after the war by the Badische Anilin und Soda Fabrik. Rhovyl, Fibravyl, Thermovyl, and Isohyl are manufactured in France from polyvinyl chloride by the Société Rhovyl.

Vinylon is the generic name for a group of polyvinyl alcohol fibers which have been treated with formaldehyde to give water resistance. All are produced in Japan. Kuralon and Cremona are spun by the Kurashiki Rayon Co., Mewlon by the Dai Nippon Spinning Co., and Kanebian by the Kanegafuchi Spinning Co.

New polyacrylic fibers include Panfaser, produced by Cassella in Germany, and Crylor, manufactured by the Société Rhodiaceta in France.

The manufacture of glass fibers is a large and substantial industry in the U.S. The first commercial processes for the production of glass fibers were developed by the Owens-Illinois Glass Co. and the Corning Glass Works in 1931. Glass fibers show very high tensile strength but are rather brittle. The two principal makes are Fiberglas and Glassfloss.

A number of new synthetic fibers in various stages of development in the U.S. are listed in Table III. This list is by no means complete, but it may be regarded as representative of the experimental and developmental work now being carried out in this field.

TABLE III. New Synthetic Fibers and Producers.

Fiber	Type	Company
X-54	Acrylic	American Cyanamid Co.
M-24	Acrylic	Tennessee Eastman Corp.
S-16	Acrylic	Industrial Rayon Corp.
Q-1200	Acrylic	Dow Chemical Co.
Dinitrile A	Vinyl	B. F. Goodrich Co.
Teflon	Fluorinated vinyl	E. I. du Pont de Nemours & Co.
Nylon 6	Polyamide	A. L. Erlanger Co.
Nylon 6	Polyamide	Allied Chemical & Dye Corp.
Nylon 6	Polyamide	American Enka Corp.
Nylon 6	Polyamide	Industrial Rayon Corp.

### Properties

Representative properties of the principal domestic synthetic fibers are summarized in Table IV. Rather wide variations may be expected in each class, depending upon the denier, type (staple or continuous), fiber length, and the testing procedures employed. The data for Acrilan, Dynel, and Vinyon HH refer to staple; for Fortisan, to continuous filament; for the remainder, to both staple and continuous filament.

Synthetic fibers are produced in the form of monofilament yarns, multifilament yarns, staple, and tow. The polymers from which they are spun usually have molecular weights in excess of 10,000. The majority of the fibers are highly crystalline in nature, and they are usually oriented by stretching to develop the desired physical properties. Highly oriented fibers have high tenacities and low extensibilities.

Substantially all the important synthetic fibers are *hydrophobic* in nature (polyvinyl alcohol gives hydrophilic fibers), while the natural and semisynthetic fibers usually are hydrophilic in nature. Owing to the limited amount of moisture absorbed by synthetic fibers, garments fashioned from them can be given semipermanent heat-set creases. In addition, such garments usually have pronounced wrinkle-resisting properties.

On the other hand, the hydrophobic characteristics of the synthetic fibers impart undesirable static properties and render them somewhat difficult to dye by normal dyeing procedures. The former difficulty can be controlled by the application of proper finishes to the fiber, while the development of new dyes and dyeing procedures is eliminating the dyeing problems.

Nylon is outstanding for strength and resistance to abrasion. The new poly-

TABLE IV. Representative Properties of Principal Domestic Synthetic Fibers.

Fiber	Tenacity, g./denier	Elonga- tion at break, %	Water absorb- ency, %	Moisture regain, % at 70°F. and r.h., 65%	Tenacity loss, wet, %	Sp.gr.	Heat resistance	Biological resistance	Chemical resistance
Viscose rayon	2.0-4.6	17-30	27	13	55	1.5	Good	Medium	Medium
Cuprammonium rayon	1.7-2.3	10-18	27	11-12	45	1.5	Good	Medium	Medium
Fortisan	4.5-6.3	6	20	11	15	1.5	Good	Medium	Medium
Acetate	1.3-1.6	20-30	14	6	40	1.3	Medium	Medium	Medium low
Vicara	1.1-1.25	38	25	10	52	1.25	Medium	Medium	Medium
Nylon	4.0-7.7	14-25	8	4	12	1.14	Medium	Excellent	Good
Vinyon HH	0.7-1.0	125	0.1	0	0	1.34	Low	Excellent	Medium low
Saran	1.4-2.3	27	0.1	0	0	1.7	Medium low	Excellent	Medium
Polyethylene	1.0-2.5	21-42	0	0	0	0.92	Low	Excellent	Medium low
Dynel	3.0	35	1	0.4	0	1.31	Medium low	Excellent	Good
Orlon	2.5	15-25	2	1	8	1.17	Medium	Excellent	Good
Acrilan	2.5-4.5	30-36	1.5	1.2	10	1.17	Medium	Excellent	Good
Dacron	3.6-5.0	15-30	0.6	0.4	0	1.38	Medium	Excellent	Good
Glass	6.3-6.9	3	0.3	0.4	0	2.5	Good	Excellent	Good

acrylic and polyester fibers have excellent warmth and warm-to-the-touch factors, and they resist the destructive action of moths, molds, mildew, and insects in general.

The hand of fabrics made from synthetic fibers is of importance from the standpoint of determining their field of usefulness. This can be varied substantially by suitable changes in spinning procedures and by use of different finishes.

The following list of outstanding properties was recently compiled by Robert Shook Associates in a survey of the synthetic fiber field:

Fiber	Outstanding property
Nylon	Abrasion resistance
Orlon	High bulk
Dacron	Great resilience
Acrilan	Bulking power, dyeing, and resistance to pilling
Dynel	Resistance to burning

It should be emphasized that all the properties listed as outstanding for individual fibers are possessed by the others to at least some degree.

The majority of the new synthetic fibers are being used in the form of blends. A recent survey has indicated that the following values can be obtained by the use of one or more of the synthetic fibers in blends containing natural fibers or the semisynthetic fibers: (1) improved wear resistance, (2) crease retention, (3) wrinkle resistance, (4) improved launderability, (5) quick drying, and (6) light weight.

### Economics

The prices of staple fibers in September, 1954, were as follows:

Dacron.....	\$1.60 per lb.
Nylon.....	1.50 per lb.
Orlon.....	1.50 per lb.
Acrilan.....	1.40 per lb.
Dynel.....	1.28 per lb.
Vicara.....	1.00 per lb.
Saran.....	0.70 per lb.

Production and use of synthetic fibers are growing rapidly. The U.S. production of noncellulosic fibers in million pounds in representative recent years is shown in Table V.

**TABLE V. Production of Noncellulosic Fibers in the U.S.**  
(In Million Pounds)

Year	Filament	Staple	Total
1940	5	—	5
1945	44	6	50
1950	121	23	144
1951	177	33	210
1952	214	49	263
1953	245	55	300

The estimate of synthetic fiber consumption in the U.S. for 1960 and 1975 recently published by the President's Material Policy Commission is given in Table VI. Although many textile technologists will regard the 1975 estimates as excessive, the production of synthetic fibers is expected to increase several-fold between now and 1975.

**TABLE VI. Estimated U.S. Consumption of Synthetic Fibers.**

Fiber	Consumption, millions of pounds	
	1960	1975
Nylon	300	800
Acrylics	325	1200
Dacron	150	1000
Miscellaneous	200	1000
<i>Total</i>	<i>975</i>	<i>4000</i>

The 1953 U.S. consumption of all fibers is shown in Table VII.

**TABLE VII. U.S. Consumption of Fibers in 1953.**

Fiber	Million pounds	Pounds per capita	%
Cotton	4519.4	27.91	69.1
Rayon and acetate	1222.9	7.55	18.7
Wool	485.8	3.00	7.4
Synthetic	300.0	1.85	4.6
Other	25.4	0.10	0.2
<i>Total</i>	<i>6553.5</i>	<i>40.41</i>	<i>100.0</i>

As would be expected, the rate of increase in the production of synthetic fibers is much greater than that of natural fibers. In certain fields of application in the textile industry strong competition exists between natural and synthetic fibers. In many cases, however, synthetic fibers have created entirely new markets, or have

supplemented the use of natural fibers in certain applications in which such fibers were deficient in quality or not available in sufficient quantities to meet the demand. Typical examples are the use of synthetic fibers in the manufacture of fabrics resistant to chemical attack, and the use of nylon in place of silk in hosiery because of its better wearing properties. Equally important have been the quick-drying, washable, form-stable, and crease-retaining properties of many of the newer synthetics.

On the other hand, certain properties of natural fibers are difficult to reproduce in synthetics. Even without taking into consideration mankind's inborn attachment to the hand and touch of natural fibers, it is safe to predict that these fibers will always play an important part in the textile field.

It is noteworthy that the advent of rayon did not result in market displacement of other fibers in the textile industry, but rather encouraged their use. Silk continued to be used in undiminished quantities until the outbreak of World War II effectively stopped all imports. A total of 29.2 million pounds of silk was consumed in the U.S. in 1920, and 35.8 million pounds in 1940. The same situation prevailed with respect to cotton, the per capita consumption increasing from 17.7 lb. in 1930 to 26.3 lb. in 1950. In other words, increasing consumption of synthetic fibers has been accompanied by a corresponding increase in the consumption of natural fibers. The products complemented each other.

The dependence of agriculture on the weather and other seasonable variations has led to wide fluctuations in the supply, quality, and price of natural fibers. While the semisynthetic fibers also are based on the use of naturally grown raw materials, adverse growing conditions usually will not have the same serious effect on their production because of the possibility of using alternative starting materials. Thus both rayon and acetate may be made readily from either cotton linters or refined wood pulp. An increase in the price of cotton linters due to scarcity or diversion to other uses will result in a greater use of wood pulp as a starting material.

Synthetic fibers are produced from readily available chemical raw materials derived from mineral sources that are unaffected by seasonable variations in weather or other natural conditions. Technical developments may be depended upon to lower manufacturing costs gradually, and only long-continued inflationary trends will result in any increase in price. As synthetic fibers are chemical products, their selling prices undoubtedly will follow the same downward trend with time so characteristic of other basic chemical commodities. Owing to increased costs for land, labor, and materials in agricultural operations, which are not so completely counterbalanced by improved operating efficiencies as are industrial operations, natural fibers have shown a fairly steady increase in price with time. Government support of prices and tariff protection also are contributing factors in maintaining natural fiber prices at fairly high levels.

These considerations lead to the conclusion that an outstanding factor in the growing use of synthetic fibers will be price stability, as natural fibers have a tendency to fluctuate rather widely in price with changing conditions affecting supply and demand. Wool, which was priced at \$1.65 per pound in 1948, jumped to \$4.00 shortly after the outbreak of the Korean war, dropped to \$3.00 by the end of 1950, and to \$1.70 in 1954. Rayon, during the same period, varied in price between the narrow limits of 36 to 40 cents per pound, and nylon was even more stable in price. Based on readily available chemical raw materials produced under highly competitive conditions, the new synthetic fibers undoubtedly will be quite stable in price and will have a moder-

ating influence on the price of other fibers. The stabilizing influence of synthetic rubber upon the price of natural rubber is a good example of what can be accomplished in this direction.

In times of international stress, a strong domestic synthetic fiber industry is an essential contribution to the total defense effort. The replacement of silk by nylon during World War II is a good example of the importance of being sufficient in all fields of utilization. As the majority of the wool used in the U.S. is imported, the development of sufficient production capacity for the manufacture of wool-like fibers to satisfy all domestic and military needs is obviously desirable.

The location of the semisynthetic and synthetic fiber production facilities in the U.S. is dictated by economic considerations. As the raw materials required for their preparation are largely obtained in the South, and the mills for converting the fiber to yarn and finished fabrics are concentrated in the same area, the majority of the plants for the manufacture of man-made fibers are located in the South. Approximately 80% of the rayon and acetate manufactured in the U.S. comes from plants in the southern states, and over 80% of all rayon and acetate manufactured domestically is processed in southern mills. The synthetic fiber industry is almost exclusively a southern industry. The basic raw materials are obtained largely from the petrochemical plants located in the southwest, and the resulting fibers are converted to finished textiles in the spinning, weaving, and finishing mills located in the southeast.

The capital investment required per annual pound of staple fiber production ranges from \$1.00 to \$1.50, while the corresponding investment for continuous filament production ranges from \$2.00 to \$2.50. It has been estimated that \$40 million for research and development is required to place a new fiber on the market on a plant-scale operation basis, and \$150 million is required to construct and operate a fiber plant for the production of 50 million pounds of fiber per year, including the cost of the auxiliary plants for producing the chemical raw materials.

Synthetic fibers are required in ever-increasing quantities to clothe the people in the world because of increasing competition between food and fiber crops for available land. During the past three centuries there has been a phenomenal growth in world population. Estimated at 400 million in 1640, it is now approximately 2¼ billion and is increasing at the rate of 1% per year. This increase has been accompanied by an equally rapid decline in the amount of land adapted to food and fiber production due to erosion, improper use, and overcultivation. The available arable land on the globe is now estimated at not more than 2½ billion acres, or slightly more than 1 acre per person. As a result, over half of the people in the world go to bed hungry each night.

The total world fiber consumption during the past few years has tended to outrun production. In fact, the supply of natural fibers would have been inadequate to meet the requirements of the textile field if substantial quantities of semisynthetic and synthetic fibers had not been available.

The world production of the four principal textile fibers—cotton, rayon, wool, and silk—was 18¼ billion pounds in 1950, the last year of free economy before the Korean war. This is identical with the world production of the same fibers in 1936 despite an increase in the production of synthetic fibers from ½ to 3½ billion pounds during the same period. As world population had increased substantially during the same period, the overall fiber supply would have been inadequate to take care of the needs of the

people if the production of synthetic fibers had not increased at a rapid rate during the same period.

In the U.S., owing to increasing competition with food crops, natural fibers seem to be approaching the upper limit of productivity. Cotton production, in particular, seems to be leveling off at 15 million bales per year. Despite every inducement by the U.S. Department of Agriculture to produce 17 million bales of cotton in 1951, and 16 million bales in 1952, only 15 million bales were ginned each year. This could develop into a serious situation if synthetic fibers were not available, since population growth will increase the total fiber requirements in the apparel and household fields alone in the U.S. by the equivalent of a million bales every  $4\frac{1}{2}$  years.

The wool industry is faced with an even more serious problem. Since the end of World War II world wool consumption has exceeded wool production by  $1\frac{1}{2}$  billion pounds.

This situation is brought into sharp focus by trends in the U.S. In 1870 there were as many sheep as there were people in the U.S.—40 million of each. By 1950 the human population had increased to over 150 million, while the sheep population had declined to 28 million. The production of domestic wool has been declining for the past decade and is now 40% less than it was in 1942. As a result, the major portion of the wool requirements of the country must be imported. In 1952, 468 million pounds of wool were consumed, but only 120 million pounds were produced.

Additional quantities of fibers must be provided to meet the needs of the growing population in the U.S., which is increasing at the rate of 7400 per day, or  $2\frac{3}{4}$  million per year. This increased fiber production must come from the synthetic fiber industry, as the quantity of land available for natural fiber production is steadily declining. It requires approximately  $2\frac{1}{2}$  acres of land per person to maintain the present standard of living in the U.S. It is estimated that by 1960 there will be less than  $2\frac{1}{2}$  acres of arable land for each person in the U.S., owing to increasing population and declining acreage resulting from improper land use and erosion. The pressure for foodstuff production will even further reduce the acreage available for growing fibers. The U.S. will need 120 million more acres of arable land by 1975. As only 30 million acres can be obtained by draining, irrigation, and clearing, the difference must be made up by increasing yields and by increasing the conversion of land from fiber production to food production.

The 1953 consumption of fibers in the U.S. was  $6\frac{1}{2}$  billion pounds, equivalent to a per capita consumption of 40 lb. At this rate of consumption, 100 million pounds of additional fibers will be required each year to meet the textile requirements of our growing population.

### Bibliography

- (1) American Viscose Corp., *Rayon Technology*, McGraw-Hill, N.Y., 1953.
- (2) Astbury, W. T., *Fundamentals of Fibre Structure*, Oxford Univ. Press, London, 1933.
- (3) Bawn, C. E. N., *The Chemistry of High Polymers*, Interscience, N.Y.-London, 1948.
- (4) Bendure, Z., and Pfeiffer, G., *America's Fabrics*, Macmillan, N.Y., 1947.
- (5) Caldwell, S. A. G., *Rayon Staple Fibre Spinning*, Emmott, London, 1953.
- (6) *Collected Papers of Wallace H. Carothers on Polymerization*, Interscience, N.Y.-London, 1940.
- (7) Garner, W., *Textile Laboratory Manual*, National Trade Press, London, 1952.
- (8) Hall, A. J., *The Standard Handbook of Textiles*, Van Nostrand, N.Y., National Trade Press, London, 1950.
- (9) Hall, A. J., *A Handbook of Textile Finishing*, London, 1952.

- (10) Hermans, P. H., *Physics and Chemistry of Cellulose Fibers*, Elsevier, Houston, Tex., 1949.
- (11) Hill, R., *Fibres from Synthetic Polymers*, Elsevier, Houston, Tex., 1953.
- (12) Hopkins, G. E., *Wool as an Apparel Fiber*, Reinhart, N.Y., 1953.
- (13) Horsfall, R. S., and Lawrie, L. G., *The Dyeing of Textile Fibers*, Behn, London, 1946.
- (14) Inderfurth, K. H., *Nylon Technology*, McGraw-Hill, N.Y., 1953.
- (15) Kaswell, E. R., *Textile Fibers, Yarns, and Fabrics*, Reinhold, N.Y., 1953.
- (16) McFarlane, S. B., *The Technology of Synthetic Fibers*, Fairchild, N.Y., 1953.
- (17) Marsh, J. T., *Textile Science*, Chapman & Hall, London, 1948.
- (18) Maurer, L., and Wechsler, H., "Man-Made Fibers," *Modern Textiles Mag.*, 1953.
- (19) Mauersherger, H. R. (ed.), *Matthews' Textile Fibers*, 6th ed., Wiley, N.Y., 1954.
- (20) Monerief, R. W., *Artificial Fibres*, Wiley, N.Y., 1954.
- (21) President's Material Policy Commission, Vol. IV, p. 200, Washington, D.C., 1952.
- (22) Preston, J. M., *Fibre Science*, 2nd ed., Textile Institute, Manchester, 1953.
- (23) Ranshaw, G. S., *The Story of Rayon*, Heinman, N.Y., 1949.
- (24) Schmidt, A. N., and Marlies, C. A., *Principles of High-Polymer Theory and Practice*, McGraw-Hill, N.Y., 1948.
- (25) Sherman, J. V., and Sherman, S. L., *The New Fibers*, Van Nostrand, N.Y., 1946.
- (26) Skinkle, J. H., *Textile Testing*, Chemical Pub. Co., N.Y., 1949.
- (27) Robert Shook Associates, *How To Buy and Sell Products Made of the New Miracle Fibers*, N.Y., 1952.
- (28) Textile Institute, *Review of Textile Progress*, Vol. 4, Manchester, 1953.
- (29) Urquhart, A. R., et al., *The Development of Some Man-Made Fibers*, Textile Institute, Manchester, 1952.
- (30) Whittaker, C. M., *The Fibro Manual*, Sylvan Press, London, 1949.

F. J. SODAY

## ACRYLIC AND OTHER VINYL FIBERS

### Acrlan, Orlon, X-51

The description of acrylic fibers in this section is confined to fibers containing more than 80% acrylonitrile. Although many different modifying monomers may be used in combination with 80% or more acrylonitrile, most of the properties and uses of fibers from these monomer combinations are largely similar. See also "Dynel and Vinyon," p. 831.

Production of acrylic fiber has been announced in both the United States and Europe by the following manufacturers with the corresponding trade-marks:

Company	Acrylic fiber trade-mark
E. I. du Pont de Nemours & Co., Inc., U.S.A.	Orlon
Chemstrand Corp., U.S.A.	Acrlan
American Cyanamid Co., U.S.A.	X-51
Suddutsche Zellwolle, Germany	Dolan
Phrix, Germany	Redon
Cassella Farbwerke, Germany	Pan
Kunstzijdespinnerij Nyma, Holland	N-53
Rhodiaceta, France	Crylor

Figure 1 shows typical cross sections of the U.S. fibers.

The low price of acrylonitrile and the possibility of further price decreases as larger-scale production gets under way have made acrylic fibers the center of considerable interest, once the fiber-forming properties of the polymer had been demonstrated. Although the companies shown above are the only ones to have announced



acrylic fibers by July 1954, a number of other fiber producers have been frequently reported working on experimental fibers. The descriptions given in the section on manufacturing reflect this wide interest.

The earliest large-scale use of acrylonitrile was in copolymers for synthetic rubbers. Polyacrylonitrile has been known in the German patent literature since the late 1920's. Being insoluble in common organic solvents and unstable in its melting range, the polymer defied early attempts to make a fiber from it. In 1938, two patents described fibers from the polymer dissolved in quaternary ammonium compounds

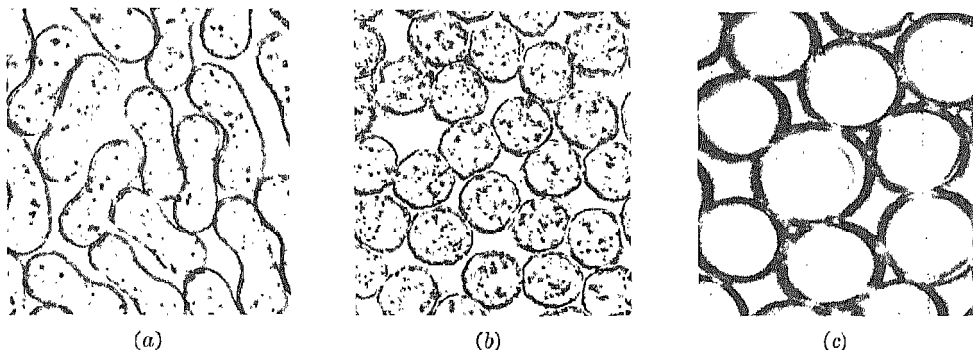


Fig. 1. Acrylic fibers ( $\times 500$ ). (a) Du Pont Orlon; (b) Chemstrand Acrilan; (c) American Cyanamid X-51.

such as benzylpyridinium chloride (11) and concentrated water solutions of metal salts such as lithium bromide, sodium thiocyanate, and aluminum perchlorate (12). None of the specific procedures described in these patents, without modification, have been demonstrated as practical for a commercially satisfactory fiber.

The first commercial acrylic fiber was introduced by du Pont in 1948 under the trade-mark Orlon. It had previously been known as Fiber A and had been in development since 1941. It had first been offered for military applications in 1942; development for civilian consumer uses was delayed until the end of World War II.

#### PHYSICAL AND CHEMICAL PROPERTIES

The density of acrylic fibers ranges from 1.135 to 1.18 depending on whether and how much comonomer is used and on the method of fiber manufacture. Tenacities are from 2 to 4 grams per denier for staple and 3 to 6 grams per denier for continuous filament. Tenacity and elongation can be controlled by the stretching process to suit individual end uses. The fiber will regain less than 2% moisture at 70°F. and 65% r.h.

Like other hydrophobic fibers, acrylic fibers are quick-drying. Creases set in fabrics of acrylic fiber are not substantially affected by moisture. The fiber has good resistance to the degradative or solvent action of common organic solvents, oils, greases, mineral acids, weak alkalies, neutral salts, and some acid salts. Its resistance to the effects of outdoor exposure is outstanding among organic fibers. For example, awnings made of a bright acrylic fiber lost less than 50% of their strength during outdoor exposure for about two years (9). Acrylic fiber is resistant to degradation by bacteria and insects. From the standpoint of flammability, it is usually ranked with cotton

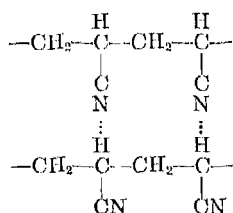
and rayon (9). A detailed discussion of the physical properties of acrylic fiber from a textile standpoint was published in 1953 (4).

#### MANUFACTURE

Acrylic fiber producers have not published process details to any great extent; this is due largely to the youth of the processes with the accompanying possibilities of rapid changes, and the fact that improved copolymer compositions are being continually investigated. This section has been selected from patents assigned to firms either producing or known to be interested in acrylic fibers.

The fiber may be produced in the usual forms of continuous filament, staple, or tow.

A feature of the structure of polyacrylonitrile is the many relatively weak attractive forces, shown by dotted lines in the adjoining figure, operating between the nitrile groups on one chain and the  $\alpha$ -hydrogens on adjacent chains.



**Polymerization.** The preferred methods of polymerizing acrylonitrile are either by emulsion polymerization in water or a modified solution polymerization method in which the monomer is dissolved in water with a suitable catalyst and the polymer product is a water slurry. These methods and other methods that are less used commercially have been surveyed by Schildknecht (8).

According to one procedure for the modified solution polymerization method, 40 grams of ammonium peroxydisulfate catalyst and 80 grams of sodium bisulfite activator are dissolved in 94 lb. of distilled water heated to 40°C. During two hours, 16 lb. of acrylonitrile are added slowly with stirring. Polyacrylonitrile with a molecular weight of about 60,000 precipitates from the solution (17). If desired, up to 20% comonomer may be added to yield a copolymer with certain desired properties.

Suitable catalysts range from the redox pairs, such as the peroxydisulfate-bisulfite system, to the peroxides, such as benzoyl peroxide (8).

Much work has been reported on copolymers that contain 20% or less of a comonomer to confer some special property on the copolymer, such as improved dyeability. Homopolymer of acrylonitrile is fairly difficult to dye. Table I represents some of the comonomers that have been described, mostly to improve dyeability; this list is by no means comprehensive.

The useful molecular-weight range for forming polyacrylonitrile fibers has been described as from 15,000 to 300,000; most polyacrylonitriles for commercial fibers have a molecular weight probably between 30,000 and 100,000, depending on the conditions of the particular spinning process.

**Spinning.** Fiber is produced from the polymer by either wet- or dry-spinning; being unstable in its melting temperature range, the polymer has not been melt-spun. The structural limitations of organic solvents for polyacrylonitrile have been well

TABLE I.

Comonomer	Reference
Itaconamide	32
N-substituted maleamic acids	33
Vinyl acetate	35
Styrene	35
Acrylamide	35
N-Vinylcarbazole	35
N-Allyl ureas	37
Isobutylene	38
N-substituted acrylamides	42
Acrylic esters	22
$\alpha$ -Substituted acrylic esters	22
Amine oxides	48
Unsaturated sulfonates	50
Vinylidene chloride	51
Fumaric acid	36
Vinyl chloride	30
2-Vinylpyridine	47

defined. Qualitatively described, these solvents are strongly polar organic molecules that break the interchain bonds of the polymer molecules between the  $\alpha$ -hydrogens and nitrile groups on adjacent chains. The solvent molecules can be visualized as being held to these two bonding sites more strongly than they hold to each other (5). Among the organic solvents that have been described are: malononitrile (21), dimethyl sulfoxide and sulfone (15), nitrophenols and nitronaphthols (18), dimethylformamide (13), aromatic diamines (17),  $\alpha$ -methoxy-*N,N*-dimethylacetamide (19), succinonitrile (14), trimethylene and ethylene thiocyanate (16), *N,N*-dimethylecyanamide (20), maleic and succinic anhydrides (27), dimethylformamide with phosphorus acids and oxides (28) and organic acids (29), ethylene carbonate (31),  $\gamma$ -butyrolactone (31), guanidine thiocyanates (34), and dimethylacetamide (52).

In *wet-spinning* acrylic fiber, the polymer is dissolved in an appropriate solvent. The resulting solution is then extruded into a bath that is miscible with the polymer solvent but precipitates the polymer in its filament form.

In one method, a 10–30% polymer solution is heated and spun into a glycerol bath heated to around 140°C. (23). The bath travel is about 24 in. and the yarn is stretched in the bath by a tension of 1.2 grams per denier. The bobbin package is washed free of glycerol with water and dried. A two-bath system may be used, in which the first glycerol bath is at 120°C. and the second glycerol bath at 170°C. A tension of about 0.9 gram per denier is applied in the second bath. The length of bath travel depends partly on the number of filaments being produced from the spinnerette: the more filaments, the longer the bath travel needed to complete coagulation.

Other liquids can be used as the spinning bath including: a 30–50% water solution of calcium chloride heated to 90°C. (24), a 10–50% water solution of a zinc halide heated to 90°C. (25), and a 12–32% thiosulfate solution heated to 100°C. (31). When ethylene carbonate is the solvent for the acrylonitrile polymer, a special spinning bath is required to circumvent the tendency of the ethylene carbonate to hydrolyze and alcoholize (44). A 20% solution of the polymer in ethylene carbonate is heated to 120°C. and extruded into a bath of 80% dipropylene glycol and 20% ethylene carbonate. The bath temperature is held at 130°C. The yarn is then washed 6–10

hours with water at 80°C., stretched about 10-fold while being heated to 150°C., and, finally, relaxed at about 140°C.

Polyalkylene ether glycols, such as triethylene glycol, may also be used as coagulants in the spinning of ethylene carbonate solutions of the polymer (43).

Another wet-spinning process provides for a spinning bath composed of water and the particular polymer solvent used. As the filaments emerge from the bath, they are washed with water which flows countercurrently into the spinning bath at a rate that is claimed to keep the bath composition fairly constant (47). The examples cited include an 18% solution of polyacrylonitrile in dimethylacetamide. The yarn is further processed by stretching at 80-85°C., washing, drying, stretching again in a tube of steam, twisting, and finally relaxing in boiling water.

Wet-spinning of hydrotropic salt solutions of the polymer, which was described earlier (12) but had not been commercially successful, has been subsequently claimed more operable if the temperature of the spinning bath is held below 10°C. (39). A 15% solution of a copolymer (containing at least 85% polyacrylonitrile) is prepared using a 55% aqueous solution of sodium thiocyanate as the solvent. The polymer solution is heated to 60°C. and spun into a water bath held at less than 10°C. The filaments are spun vertically downward into the bath, then travel around a roller at the bottom, and are brought back up to emerge from the bath after a travel of about 36 in. These filaments are stretched about 13-fold in water at 95°C. The filaments are claimed to dye well if they are dyed while still wet from the stretching bath. If the filaments are to be dried before dyeing, treatment with a 50% water solution of a humectant, such as triethylene glycol, is described as a predrying finish necessary to obtain the same dyeability as with the wet filaments after stretching.

This cold bath process has been made continuous (40) to include spinning, stretching, application of an antistatic finish, and twisting onto a package. The eventual shrinkage of yarn prepared by this process is controlled by passing the dry yarn in a relaxed condition through a heated area ranging from 100 to 500°C., the actual temperature being determined by the length of time during which the yarn is heated (41).

The *dry-spinning* process for making polyacrylonitrile yarn is basically similar to the acetate process. The polymer is dissolved in any appropriate organic solvent to form a solution containing at least 10% solute. This solution (18) is heated, the temperature depending on the boiling point of the solvent to be evaporated, and then extruded into a heated spinning cell. A heated evaporative medium such as air, nitrogen, steam or a combination of these, moving countercurrent to the path of travel of the freshly formed filaments, removes the solvent and carries it out of the spinning cell to be recovered. The filaments are rewound after being stretched 3- to 10-fold between draw rollers. During the drawing process, the yarn is heated by passing it around a heated pin or through a heated medium such as air or water. The temperature range during drawing varies from 100 to 250°C., depending on the actual time of contact during heating.

In addition to the use of copolymers to improve dyeability, various other methods have been tried for the same purpose. For example, treatment of either the polymer solution or the yarn with hydrazine or a hydrazine salt has been described (26).

Mixtures of polymers have also been used. Copolymerization (using more than one type of monomer) usually yields a polymer with a melting range lower than the homopolymer. Polymer mixtures that have been claimed to have the advantage of

increased dyeability while preserving high melting ranges are: polyacrylonitrile and the copolymer of isopropenyl acetate and vinyl acetate (45), polyacrylonitrile and the homopolymer of methyl  $\alpha$ -acetaminoacrylate (49), and polyacrylonitrile and the copolymer of maleic anhydride and vinyl acetate (46).

#### ECONOMIC ASPECTS

Because of the low cost of acrylonitrile and the prospect of further cost cuts, it has been predicted that eventually only the cellulosic staple fibers will be lower-priced than staple fibers containing acrylonitrile (1) and that acrylic fibers will consume, by 1955, 60% of the acrylonitrile output (10). It has been pointed out (6) that most of the future fiber research activity will probably center around acrylic fibers.

#### USES

Acrylic fibers have properties that have been found useful in applications ranging from coats and suits, through work clothes, to automobile convertible tops, awnings, and curtains.

Blends of acrylic fiber with other fibers, both natural and man-made, are extensively used in men's and women's outer apparel such as suits, skirts, and coats, and in blankets, sportswear, and dress goods. The acrylic fiber contributes to the blend a number of advantages, including crease retention, recovery from wrinkling, stabilization against shrinkage, and dimensional stability during changes in humidity. If desired, fabrics can be constructed to take advantage of the bulkiness and high covering power of acrylic fiber.

Fabrics of 100% acrylic fiber have been used in shirts, blouses, underwear, knitted wear, work clothing, and curtains. Work clothing of acrylic fiber has been worn for unusually long periods in areas where acid caused former work clothes to deteriorate rapidly. Curtains of acrylic fiber take advantage of the high resistance of the fiber to the effects of weathering and outdoor exposure; this is also the case with acrylic fiber convertible tops for automobiles and awnings.

In shirts, blouses, and underwear, continuous filament provides a soft, dry feel along with resistance to stretch, easy launderability, rapid drying, and high strength. Knitted wear of acrylic fiber has a pleasant feel, good shape retention, and resistance to attack by moths. The fiber has also been used for home knitting yarns.

Industrially, the fiber may be used where chemical stability and resistance to weathering is needed, for example, in filter cloths, dust collection bags, tents, tarpaulins, anode bags, agricultural and mine belting, and diaphragm fabric.

One of the biggest problems that was overcome in using acrylic fiber for apparel was dyeability. Besides the copolymer and mixed polymer approach mentioned earlier, new dyes (6a) and new dyeing methods have also been developed (2,3,4).

#### Bibliography for Acrilan, Orlon, X-51

- (1) Bendigo, C. W., *Chem. Eng. News*, **30**, 2810 (1952).
- (2) Blaker, R. H., *Modern Textiles Monthly*, **33**, No. 11, 46 (1952).
- (3) Feild, T. A., Jr., and Fremon, G. H., *Textile Research J.*, **21**, 531 (1951).
- (4) Fremon, G. H., "Synthetics—Vinyl Fibers," in McFarlane, *Technology of Synthetic Fibers* Fairchild Publications, N.Y., 1953, p. 135.
- (5) Houtz, R. C., *Textile Research J.*, **20**, 786 (1950).

- (6) McFarlane, S. B., "Fibers of the Future," in McFarlane (see ref. 4), p. 371.
- (6a) Meunier, P. L., Laucius, J. F., Brooks, J. A., and Thomas, R. J., *Am. Dyestuff Repr.*, **42**, P470 (1953).
- (7) Quig, J. B., *Papers Am. Assoc. Textile Technol.*, **4**, No. 2, 61 (1949).
- (8) Schildknecht, C. E., *Vinyl and Related Polymers*, Wiley, N.Y., 1952, pp. 256-286.
- (9) *Technical Manual for "Orlon" Acrylic Fiber*, E. I. du Pont de Nemours & Co., Inc.
- (10) Weith, A. J., *America's Textile Repr.*, **67**, No. 25, 19 (1953).
- (11) U.S. Pat. 2,117,210 (May 10, 1938), H. Rein (to I. G. Farbenind.).
- (12) U.S. Pat. 2,140,921 (Dec. 20, 1938), H. Rein (to I. G. Farbenind.).
- (13) U.S. Pat. 2,404,714 (July 23, 1946), G. H. Latham (to du Pont).
- (14) U.S. Pat. 2,404,715 (July 23, 1946), A. O. Rogers (to du Pont).
- (15) U.S. Pat. 2,404,717 (July 23, 1946), R. C. Houtz (to du Pont).
- (16) U.S. Pat. 2,404,718 (July 23, 1946), R. C. Houtz (to du Pont).
- (17) U.S. Pat. 2,404,720 (July 23, 1946), R. C. Houtz (to du Pont).
- (18) U.S. Pat. 2,404,721 (July 23, 1946), R. C. Houtz (to du Pont).
- (19) U.S. Pat. 2,404,724 (July 23, 1946), R. C. Houtz (to du Pont).
- (20) U.S. Pat. 2,404,725 (July 23, 1946), A. O. Rogers (to du Pont).
- (21) U.S. Pat. 2,404,727 (July 26, 1946), R. C. Houtz (to du Pont).
- (22) U.S. Pat. 2,412,034 (Dec. 3, 1946), G. F. D'Alelio (to General Electric).
- (23) U.S. Pat. 2,426,719 (Sept. 2, 1947), W. W. Watkins (to du Pont).
- (24) U.S. Pat. 2,451,420 (Oct. 12, 1948), W. W. Watkins (to du Pont).
- (25) U.S. Pat. 2,467,553 (April 19, 1949), W. A. Hare (to du Pont).
- (26) U.S. Pat. 2,497,526 (Feb. 14, 1950), H. W. Arnold (to du Pont).
- (27) U.S. Pat. 2,498,605 (Feb. 21, 1950), G. E. Ham (to Monsanto Chemical Co.).
- (28) U.S. Pat. 2,503,244 (April 11, 1950), H. W. Coover, T. E. Stanin, and J. B. Dickey (to Eastman Kodak).
- (29) U.S. Pat. 2,503,245 (April 11, 1950), H. W. Coover, T. E. Stanin, and J. B. Dickey (to Eastman Kodak).
- (30) U.S. Pat. 2,515,206 (July 18, 1950), T. G. Finzel and G. F. D'Alelio (to Industrial Rayon).
- (31) U.S. Pat. 2,530,962 (Nov. 21, 1950), W. A. Hare (to du Pont).
- (32) U.S. Pat. 2,531,410 (Nov. 28, 1950), G. F. D'Alelio (to Industrial Rayon).
- (33) U.S. Pat. 2,533,204 (Dec. 12, 1950), J. R. Caldwell (to Eastman Kodak).
- (34) U.S. Pat. 2,533,224 (Dec. 12, 1950), A. W. Cresswell (to American Cyanamid).
- (35) U.S. Pat. 2,537,031 (Jan. 9, 1951), D. W. Chaney (to American Viscose).
- (36) U.S. Pat. 2,541,011 (Feb. 13, 1951), J. R. Caldwell (to Eastman Kodak).
- (37) U.S. Pat. 2,544,638 (March 13, 1951), J. R. Caldwell (to Eastman Kodak).
- (38) U.S. Pat. 2,549,913 (April 24, 1951), M. R. Lytton (to American Viscose).
- (39) U.S. Pat. 2,558,730 (July 3, 1951), A. Cresswell (to American Cyanamid).
- (40) U.S. Pat. 2,558,731 (July 3, 1951), A. Cresswell (to American Cyanamid).
- (41) U.S. Pat. 2,558,733 (July 3, 1951), A. Cresswell and I. Wison (to American Cyanamid).
- (42) U.S. Pat. 2,560,680 (July 17, 1951), A. L. Allewelt (to American Viscose).
- (43) U.S. Pat. 2,570,200 (Oct. 9, 1951), H. A. Bruson (to Industrial Rayon).
- (44) U.S. Pat. 2,570,201 (Oct. 9, 1951), H. A. Bruson and G. S. Hooper (to Industrial Rayon).
- (45) U.S. Pat. 2,571,777 (Oct. 16, 1951), T. E. Stanin and J. B. Dickey (to Eastman Kodak).
- (46) U.S. Pat. 2,575,006 (Nov. 13, 1951), H. W. Coover, Jr., and J. B. Dickey (to Eastman Kodak).
- (47) U.S. Pat. 2,577,763 (Dec. 11, 1951), H. M. Hoxie (to American Viscose).
- (48) U.S. Pat. 2,586,238 (Feb. 19, 1952), M. R. Lytton (to Chemstrand).
- (49) U.S. Pat. 2,589,055 (March 11, 1952), H. W. Coover, Jr., and J. B. Dickey (to Eastman Kodak).
- (50) U.S. Pat. 2,601,256 (June 24, 1952), H. A. Bruson (to Industrial Rayon).
- (51) U.S. Pat. 2,610,173 (Sept. 9, 1952), G. E. Ham (to Monsanto Chemical Co.).
- (52) U.S. Pat. 2,649,427 (Aug. 18, 1953), C. S. Marvel (to du Pont).

P. M. LEVIN

### Dynel and Vinyon

Dynel is an acrylic synthetic fiber, manufactured by Carbide and Carbon Chemicals Company, a division of Union Carbide and Carbon Corporation. It is composed of 60% vinyl chloride (see *Vinyl compounds*) and 40% acrylonitrile (*q.v.*). Ultimate raw materials for Dynel are natural gas, ammonia, salt, and air.

In the early 1930's, large strides were made in the field of synthetic vinyl resins and plastics. Most promising of these resins were those of the vinyl chloride family and, fortuitously, it was observed that this group could be readily formed into fibers. In view of this discovery, a separate research department section was established by Union Carbide and Carbon Corporation to work specifically on textile fibers. In this work, three basic factors had to be considered. To produce a practical textile fiber: (1) the molecules comprising it had to be at least 1,000 Å. long; (2) they had to be oriented essentially parallel to the fiber axis; and (3) they had to exhibit crystallite structure to a considerable extent. In addition, of course, the fiber had to have functional merit in order to compete with and improve upon the existing natural and semi-synthetic fibers. Vinyon continuous filament, the first product approaching these qualifications, was introduced in 1936. It was produced by American Viscose Corporation from a copolymer of vinyl chloride and vinyl acetate made by Union Carbide.

Vinyon filament had a number of excellent properties: high strength, water and chemical resistance, and moth- and mildewproofness, but it also had two major defects: (1) its high chemical resistance made it difficult to dye; (2) its softening point of 65°C. (149°F.) was too low.

Strangely enough, one of the so-called defects led to the fiber's largest market. The low softening point made later Vinyon fibers suitable for the production of sculptured carpet fabrics, nonwoven fabrics, paper, felts, and other such specialized products where the application actually depended upon the thermoplasticity of the fiber. However, inability to withstand boiling water permanently relegated Vinyon fibers to specialized uses.

At present, only a cut staple variety of Vinyon is produced. Known as Vinyon HH, the fiber's market is in the neighborhood of a million pounds per year, for uses as described above. Development work continued then with the goal of bettering fiber properties and, in particular, building up resistance to boiling water. In 1946, a fiber possessing such improvements was dry-spun from a copolymer of 60% vinyl chloride and 40% acrylonitrile. It was called Vinyon N continuous filament (6).

Vinyon N filament found ready application to limited end uses requiring exceptional strength and chemical resistance, such as filter fabrics, special work clothing, airplane trim cloth, resist yarns, and special sewing threads. However, the fiber's susceptibility to heat and, more important, the difficulty in producing it in a low-cost continuous process, relegated it to secondary importance and it is no longer produced. Work done on Vinyon N, however, was destined to lead to a major development in the textile market. In 1949, the streamlining of a production process, its application to the production of staple fiber rather than continuous filament, and improvements made in the copolymer resulted in the introduction of the new acrylic, Dynel.

### PROPERTIES

Dynel is characterized by good dry and wet strength, dimensional stability, warmth, resilience, rapid drying, exceptional resistance to both combustion and chem-

ical degradation, moth- and mildewproofness, and thermoplasticity. The fiber's identifying properties are given in Table I. A cross section of Dynel fiber is shown in Figure 1 and an x-ray diffraction diagram of Dynel in Figure 2.

TABLE I. Properties of Dynel.

Filament shape.....	Irregular ribbon-shaped cross section accounting for its high covering power
Sp.gr. (at 81°F.).....	1.31
Tenacity, wet or dry, g./denier.....	3.0
Elongation, wet or dry, %.....	.36
Average stiffness, g./denier.....	9.7
Average toughness, g./denier.....	0.52
Flammability.....	Fire-resistant; will not support combustion; shrinks from flame and does not melt or drip
Moisture regain, %, at 78°F. and 60% r.h.....	Less than 0.4
Resistance to chemicals.....	Excellent for strong detergents and soaps, and a wide variety of inorganic acids, bases, and salts
Resistance to solvents.....	Unaffected by hydrocarbons and most organic solvents. Acetone, cyclohexanone, and dimethylformamide are solvents in varying degrees. Certain ketones and amines exert solvent or swelling action at higher temperatures
Resistance to insects.....	Excellent, completely resistant to the carpet beetle and clothes-moth larvae
Resistance to mildew and fungus.....	Excellent
Effect of dry heat.....	Strain release starts at 250°F.; softening range is 300-325°F.
Electrical properties.....	Medium-grade dielectric; comparable to cellulose acetate and nylon under normal conditions

The color of the "natural" fiber is a light cream. This color may be diminished to a considerable degree by bleaching with an acid solution of sodium chlorite at tempera-

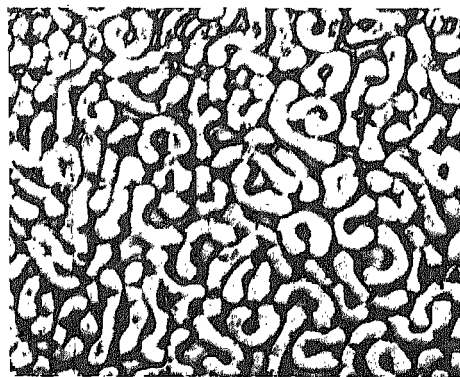
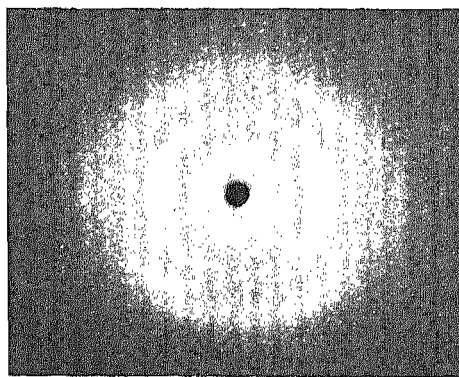
Fig. 1. Cross section of Dynel fiber ( $\times 300$ ).

Fig. 2. X-ray diffraction diagram of Dynel fiber.

tures above 194°F. (90°C.) for short periods of time or at lower temperatures by employing longer exposures. Dynel is also spun with a number of standard colors.



## MANUFACTURE (5)

**Fiber Production.** The copolymerization of the vinyl chloride and acrylonitrile monomers comprising the Dynel resin is accomplished by an emulsion process similar to that used for the copolymerization of butadiene and styrene, and also similar to other copolymerization reactions involving vinyl chloride. In sharp contrast to the readiness with which other vinyl compounds and acrylic compounds polymerize and copolymerize, the vinyl chloride-acrylonitrile copolymerization reaction tends to proceed slowly under ordinary conditions, but it can be accelerated by catalyst systems of the redox type, and controlled by means of the usual degraders and modifiers. The copolymerization ratio of vinyl chloride and acrylonitrile is rather high in favor of the latter, and it is necessary to feed acrylonitrile continuously during the reaction in order to obtain resins of the degree of compositional uniformity desired for fiber applications. At the completion of copolymerization, the resultant resin is coagulated, washed, and dried; and it emerges as a white, fluffy powder.

The dried resin is then dissolved in acetone and extruded through a multiholed spinneret into an aqueous coagulating bath. From this bath, Dynel emerges as a rope of many filaments, called tow. It is then stretched to from five to fifteen times its original length. This stretching accounts for the final tenacity and elongation characteristics of the fiber. Next, the fiber is annealed or baked to relieve strains and reduce subsequent shrinkage. Finally, it is crimped, cut, and baled for shipment.

Dynel staple is currently supplied in deniers of 2, 3, 6, 12, and 24 and cut in standard lengths from 1 to 6 in. The fiber is also available in tow form for specialized applications, such as doll wigs and carpeting, as well as for processing on the Pacific converter. Priced at \$1.28/lb. (March 1954), it is likely that Dynel will always be the most economical of the major synthetic fibers, excluding the cellulose and protein-base fibers.

**Fiber and Fabric Analysis.** The increased importance of fiber blends has naturally given rise to questions concerning the uniformity of the blend and the contribution of each fiber to the blend. To answer these questions, a method has been developed to separate the component fibers after the blend has been made. If, for example, the rayon is dissolved by sulfuric acid from a creased Dynel and rayon fabric, the Dynel skeleton or "inner structure" will be disclosed (3). A study of this inner structure has helped to answer a number of questions regarding Dynel's contribution to a participation in blends. Such elements as fiber distribution, effectiveness of union dyeing, dimensional stability, and the effects of resin treatments and high ironing temperatures upon the various components in a blend have been successfully analyzed by this technique.

**Dyeing and Finishing (2).** Much of the success of all-Dynel and Dynel-blend fabrics depends upon the proper dyeing and finishing of the cloth. Each operation, although having certain basic qualifications, nevertheless can be handled with comparative ease. There are three requirements for the successful dyeing and finishing of Dynel. These are: (1) the use of dyeing temperatures above 205°F.; (2) restoration of the luster of the dyed fibers; and (3) consideration for the fact that the fiber is thermoplastic. The 205°F. figure has been chosen because at this temperature Dynel's water absorption becomes of practical value in dyeing. Normally, the fiber possesses very low absorption, but at high temperatures, water penetrates the fiber, thus permitting the dye to enter the fiber. When cooled again to ordinary temperatures, the color is fixed in the fiber in such a manner that unless the fiber is

again heated, the color is completely inert to the action of water and the various chemical agents that might be expected to discharge or alter the color. This results in dyeings with a high degree of wet fastness and general resistance to chemicals and gas fading. It also provides the means for obtaining unusual dye-resist and cross-dye effects in blends containing Dynel.

This tendency of Dynel to absorb water at high temperatures is responsible for the second requirement—luster restoration. The absorption of water causes the fiber luster to dull, thus markedly influencing the color value. To restore the fiber's normal semibright luster and to protect against off-shade dyeings, it is necessary to subject all-Dynel fabrics to drying temperatures around 240°F. and Dynel-rayon blends to 300°F. Relustering of Dynel-wool blends is accomplished often in the steam deating and carbonizing operations.

The importance of the thermoplasticity of the fiber may be seen in the effect of overquick cooling of the dye bath containing a Dynel fabric. Unless the temperature of the bath is gradually reduced, the thermoplastic nature of Dynel will cause it to accept and retain wrinkles formed during the dyeing operation. Slow cooling eliminates this problem.

*Types of Dyes.* Dynel has been successfully dyed with acetate, acid, direct, basic, and some vat colors. The acetate dyes (*q.v.*) are easiest to apply and possess fine leveling qualities. They are capable of producing most of the shades desired on Dynel with adequate fastness for most end uses. In the dyeing of heavy shades, sodium sulfate is often added to the dye bath to improve color exhaustion. Optimum results are attained when the dyes are well dispersed in the bath and when this is accomplished through use of a minimum amount of a dispersant.

Some of the acid dyes are capable of producing more brilliant shades than the acetate colors. Pastel shades may be obtained without using any dye assistants. Medium shades, however, greatly benefit from the slow addition of reduced copper to the dye bath, and deep shades require both reduced copper and a swelling agent, such as *p*-phenylphenol.

**Finishing.** In the finishing of Dynel fabrics, the thermoplasticity of the fiber once again is a major factor. Since Dynel is affected by high temperatures, it can be heat-set. If Dynel fabrics are stretched while hot (240–260°F.), the full amount of the stretch will not be permanently retained, but as much as 50% of it may be if the fabric is heated under tension to temperatures of the order of 270°F. Simple stretching without subsequent heat treatment is to be avoided if the fabric is to have good stability.

Dynel's high elasticity and delayed recovery from stretching also play large parts in the finishing operation. A portion of the increased fabric width, resulting from the mill practice of cold-stretching, is recovered immediately after the release of tensions because of the fiber's elasticity. Another portion may remain in the fabric and be recovered only when the fabric is heated, as in pressing. This delayed recovery factor must be carefully considered because of its effect on dimensional stability. Methods for complete relaxation of various Dynel-blend fabrics have now been worked out, based on these principles, so that extremely stable fabrics can be produced.

#### ECONOMIC ASPECTS

In the latter part of 1953, the demand for Dynel from the manufacturers of its some thirty end-product applications, as well as from those whose Dynel uses were in

developmental stages, necessitated an increase in fiber production. To facilitate this increase, the Vinyon N operation was brought to a close and the manufacturing space was converted to the production of Dynel. This change-over has raised fiber output to the level of 5,000,000 lb. per year. It is planned (1954) to build a major plant at Spray, North Carolina, to produce 20,000,000 lb. of fiber per year.

Research effort is being expended in the development of new finishes and finishing procedures, of new dyeing and stabilization methods, and of a permanent antistatic, to be applied, not on the surface, but by the incorporation of an antistatic agent in the fiber as it is being spun.

#### USES

Although Dynel resembles wool in its stress-strain curve and, therefore, is particularly applicable to the woolen and worsted systems of spinning, it is as readily adapted to other conventional spinning systems, such as cotton, silk, and jute. A few adjustments of equipment and settings to allow for the bulkiness of Dynel, as compared to the natural fibers and rayon, is all that is required to turn out spun yarns of Dynel or of blends of Dynel with other fibers.

Proper choice of the denier or size of the Dynel fibers used and a choice of spinning systems make it possible to construct fabrics ranging from the coarseness of mohair to the softness of cashmere. A review of present end uses points up this textural diversity. Dynel is used in bed and baby blankets, comforters, draperies, furlike trim for jackets and snowsuits, boys' slacks and surcoats, men's suits and slacks, work clothing, fleecy coats, dresses and blouses, lingerie, sleepwear, underwear, filter fabrics, sail cloth, chemical-resistant clothing, water-softener bags, paint-roller covers, and doll wigs.

Dynel contributes a distinctive fabric hand and also other meritorious functional characteristics. To woven goods, for instance, Dynel imparts warmth, washability, strength, good draping qualities, lasting crease retention, and long useful wear life. In knit goods it affords shape retention, dimensional stability, lasting loft and resilience, and resistance to matting.

**100% Dynel.** 100% Dynel blankets and draperies are warm, mothproof, flame-resistant, and washable, with minimum shrinkage. All-Dynel filter cloths, paint-roller covers, and work clothing have exceptional chemical resistance. Further applications of 100% Dynel in the apparel field, such as men's half hose and deep pile fabrics, show the fiber's warmth, resilience, and launderability.

**Blends.** In blends, Dynel and the auxiliary fibers are balanced to present optimum fabric qualities. For example, in woven apparel blends with cotton, Dynel improves fabric hand and gives crease and shape retention and lasting warmth, while cotton offers absorbency, low fiber price, and permits the use of a wider range of ironing temperatures. In wool and Dynel blends, wool affords traditional handle and drape whereas Dynel increases the strength and abrasion resistance of the fabric and imparts lasting crease and press retention, even when wet. Rayon blends also profit from the inclusion of Dynel, which adds strength, press and crease retention, and long wear life and permits a wide variety of color combinations and textures.

#### Bibliography for Dynel and Vinyon

- (1) Bunn, H. S., *Textile Fiber Development*, Papers of the American Association of Textile Technologists, December 1950.
- (2) Feild, T. A., Jr., *Am. Textile Repr.*, 67, No. 34, 77 (1953).

- (3) Feild, T. A., Jr., Setterstrom, C. A., and Davisson, C. W., *Am. Dyestuff Repr., Proc. Am. Assoc. Textile Chemists Colorists*, May 10, 1954.  
 (4) McCormick, J. H., *Textile Bull.*, Nov., 1953.  
 (5) Maucrsberger, H. R., *The American Handbook of Synthetic Textiles*, Textile Book, N.Y., 1952.  
 (6) Rugeley, E. W., Feild, T. A., Jr., and Fremont, C. H., *Ind. Eng. Chem.*, **40**, 1724 (1948).

II. L. CAROLAN

### Saran

Saran is the generic name for a system of polymers and copolymers produced by The Dow Chemical Co., in which vinylidene chloride is the major constituent. Saran has many unusual properties that make it particularly well-suited for textile applications. It is produced as monofilament in a range from 5 to 60 mils in size. In this range, particularly in sizes from 5 to 20 mils, it is commercially produced for the following applications: automobile seat covers, outdoor furniture, shade umbrellas, filter fabrics, insect screens, and tobacco shade cloths.

From the multifilament, staple fibers, and smaller-sized monofilaments, fabrics are produced that have a softer hand and thus are suitable for drapery and upholstery fabrics, casement cloths, rugs and carpeting, filter cloths, and also for doll hair.

The Dow Chemical Co. has licensed the following companies to produce Saran fibers:

Multifilaments, Staple,  
and Monofilaments,  
Diameter Less Than  
4 Mils

Saran Yarns Co.,  
Odenton, Md.  
Trade Name: Saran  
Firestone Plastics Co.,  
Pottstown, Pa.  
Trade Name: Velon  
National Plastics  
Products Co.,  
Odenton, Md.  
Trade Name: Saran  
by National

Bolta-Saran, Inc.,  
Lawrence, Mass.  
Trade Name: Boltaflex Saran  
Dawbarn Brothers, Inc.,  
Waynesboro, Va.  
Trade Name: Dawbarn  
Firestone Plastics Co.,  
Pottstown, Pa.  
Trade Name: Velon

Monofilaments, Minimum Diameter 4 Mils

Lus-Trus Extruded Plastics, Inc.,  
Ann Arbor, Mich.  
Trade Name: Lus-Trus  
National Plastic Products Co.,  
Odenton, Md.  
Trade Name: Saran by National  
Oriented Plastics,  
Ridgefield, Conn.  
Trade Name: Oriented

Vinylidene chloride (1,1-dichloroethylene),  $\text{CH}_2:\text{CCl}_2$ , has been known for more than 100 years. However, extensive work on polymer and copolymers has been carried out only since about 1930. This work resulted in the introduction to the plastics industry in late 1939 of a family of thermoplastics known as Saran.

Saran was first introduced to the textile trade as monofilaments 0.01, 0.012, and 0.015 in. in diameter. The most significant uses of Saran in this form are in insect screening, upholstery fabrics, woven tapes and fabrics for outdoor furniture, automotive seat covers, and brush bristles. Shortly after Saran monofilaments were commercially introduced, development of finer filaments for textile purposes was begun. This development had progressed by the beginning of World War II to a small semiplant stage. Because of the chemical resistance of Saran, this small production was absorbed in the war effort and further developmental work was delayed. After World

War II, The National Plastic Products Co. became interested in the finer Saran filaments and undertook an extensive research program. As a result of this work The Saran Yarns Co. was formed, being jointly owned by The National Plastic Products Co. and The Dow Chemical Co. Shortly after the formation of this company, production of fine Saran filaments was begun.

### PROPERTIES

The properties of the larger monofilaments and the finer-denier Saran are the same with the exception that somewhat higher tensile strengths are achieved in monofilament. Tensile strengths, depending upon diameter, are up to 50,000 p.s.i. Higher tensile strengths can be achieved but are not now being used commercially.

Saran is available as:

#### Monofilaments

Round: 0.005, 0.008, 0.010, 0.012, 0.015, 0.020, 0.030 in. and larger

Flat and oval: 0.005  $\times$  0.020 in., 0.008  $\times$  0.020 in., 0.013  $\times$  0.030 in.

#### Fibers and multifilaments

Multifilament yarns: 750/50, 900/6, 1488/12, 4500/100, 5400/200

Staple, straight: 10, 22, 30, 45, 60, 70 denier

Staple, curled: 22, 30, 45, 70 denier

Staple length for both straight and curled staple: 2-60 in.

Techniques have been developed whereby a curl (crimp) can be imparted to the fiber so that this Saran looks and feels like wool. The fibers are essentially circular in cross-section. The physical properties of Saran are given in Tables I-III. The properties listed are the results of tests performed on fibers and yarns taken from present pro-

TABLE I. General Physical Properties of Saran.

Property	Value
Color	Light straw yellow
Luster	Bright or semidull
Refractive index	1.60
Sp.gr.	1.70 $\pm$ 0.05
M.p.	340-350°F. (171-177°C.)
Moisture sorption	Less than 0.1% after immersion for 24 hr.
Temperature effects, <sup>a</sup> % shrinkage in air	
122°F. (50°C.)	1-2
158°F. (70°C.)	5-6
212°F. (100°C.)	10-15

<sup>a</sup> Untreated multifilament yarn sample.

TABLE II. Tenacity, Tensile Strength, and Elongation of Saran.

Property	Value
Tensile strength (wet or dry), p.s.i.	Up to 50,000
Breaking elongation, %	15-25
Stiffness (modulus of elasticity)	
Initial, g./denier	6-10
Average, g. per denier	8-12
Toughness index, <sup>a</sup> g.-cm./denier-cm.	0.125
Stretch resistance (5% elongation), g.-cm./cm.-denier	0.01

<sup>a</sup> Measured by area under stress strain curve.

duction. It is possible that certain of these values will be modified slightly with changes in production techniques.

TABLE III. Tensile Recovery of Saran.<sup>a</sup>

Property	Value			
Total elongation, %	1	3	5	10
Stress, g./denier	0.07	0.20	0.36	0.84
Immediate elastic recovery, %	70.0	68.5	60.0	41.0
Permanent set after 5 min. rest, %	0.0	0.0	3.0	7.0
Delayed recovery after 5 min. rest, %	30.0	31.5	37.0	52.0
Total recovery after 5 min. rest, %	100	100	97.0	93.0
Degree of resilience <sup>b</sup>	—	—	0.75	—
Flex life <sup>c</sup>	Excellent			

<sup>a</sup> Data obtained on typical continuous filament yarns using an Instron tensile tester under the following conditions: gage length, 10 in.; rate of elongation, 5 in./min.; removal of elongation, immediately after extension and at the same rate of extension; temperature, 70°F.; relative humidity, 65%.

<sup>b</sup> Recoverable work divided by total work.

<sup>c</sup> Resistance to degradation by flexing.

**Chemical Properties.** Saran yarns exhibit outstanding resistance to acids and alkalies with the exception of ammonium hydroxide. The yarns are not affected by alcohols or aliphatic hydrocarbons. Aromatic hydrocarbons, halogenated hydrocarbons, ketones, esters, and ethers may be detrimental in varying degrees. Temperature is an important factor in the effects of any of these compounds.

The moth and mildew resistance is excellent. Saran filaments are self-extinguishing. When exposed to a flame, the filaments will first shrink, then melt, and then chemically decompose. The flameproof properties of Saran have been accepted and approved by the Board of Standard and Appeals for New York City.

Saran exhibits excellent resistance to degradation by outdoor exposures, but after prolonged exposure to sunlight there is a tendency to darken. This darkening is an object of extensive research by the Dow Chemical Company and its licensees. New formulations of improved light stability are being offered as of 1954.

#### MANUFACTURE

The vinylidene chloride monomer (see Vol. 3, p. 786) is prepared by chlorinating ethylene to 1,1,2-trichloroethane and treating this with aqueous alkali. Thus the basic raw materials for Saran are petroleum and brine.

Vinylidene chloride can be easily polymerized in mass, emulsion, or suspension to form a long, linear straight-chain polymer with a structure  $(-\text{CH}_2\text{CCl}_2-)_n$ . The polymer is white and porous with a melting range of 365–392°F. (185–200°C.) and a decomposition point of about 437°F. (225°C.). To utilize this polymer as a plastic material in the ordinary sense is difficult because of its high softening point range, its tendency to evolve hydrogen chloride at the fabrication temperature, and its lack of compatibility with plasticizers in general. It appears that the properties of this polymer are best modified for general use by copolymerization. By control of the copolymerizing agents and the conditions of polymerization, a group of copolymers can be obtained with a wide range of characteristics. Further aids are needed, however, to produce a salable product. Plasticizers are used to further widen the range between

the melting point and decomposition point, as well as to give ease of extrusion. As would be expected from the chemical resistance of Saran, the extent of plasticization is limited. The types of plasticizers are limited because of their effects on heat and light stability.

The degradation of Saran polymers can be likened to that of polyvinyl chloride. The loss of hydrogen chloride creates a system of conjugate double bonds similar to those in the carotenoid color bodies. To prevent this discoloration both heat and light stabilizers are used.

#### FABRICATION, DYEING, AND PROCESSING

The Saran extrusion-grade polymers can be said to exist in three modifications: *crystalline*, the normal "as polymerized" state, giving a sharply defined x-ray pattern but also known to be partly amorphous; *amorphous*, soft, easily deformed material obtained by fusing and rapid cooling; reverts to the crystalline form at a rate depending upon time and temperature and will maintain its amorphous condition at low temperatures longer than at high temperatures; *oriented crystalline*, tough, strong, showing characteristic x-ray fiber pattern produced by plastically deforming amorphous material.

For fibers and filaments the oriented crystalline state is desirable since unidirectional properties of high tensile strength, great flexibility, long fatigue life, and good elasticity are of the utmost importance.

The fabrication of Saran polymers into fibers and filaments is accomplished by melt-spinning. A screw-type extrusion unit is used. The screw flights or the threaded section of the screw act as a conveying unit that compacts and advances the polymer to the torpedo zone where melting takes place. In melting, the plastic temperature must be sufficiently high to destroy the crystalline structure of the polymer so that a totally amorphous Saran will be extruded. The molten polymer is forced through a spinnerette and rapidly quenched to maintain the amorphous state. The bath consists of a nonsolvent material maintained at a temperature sufficiently low that crystallization will not be started. See also refs. (3,4).

Orientation is obtained by deforming the amorphous Saran by means of stretching rolls operating at different rates of speed while partial recrystallization takes place. The crystallites are thus oriented along the major axis of the fiber. The reduction in cross-sectional area is approximately proportional to the elongation which takes place and which usually is 200–300%.

Saran, since its introduction in the form of monofilaments, has been colored by pigmentation. When finer filaments and staple became available, they too were pigmented or "spun-dyed." A wide range of spun-dyed colors are available today. Colors can be custom-made to meet individual customer requirements. The fastness characteristics of the spun-dyed colors depend on the fastness of the dyes and pigments used, and therefore will vary from color to color. In general, the fastness properties are excellent on medium to dark shades. Some pastel shades tend to be fugitive.

Since Saran is noted as being relatively inert to most acids, alkalies, and solvents, it was rather surprising to find that it could be so readily dyed. The dispersed or acetate-type dyes give the best results. This class of dyes gives good color values, good penetration, and good exhaustion. By proper selection of dyes, colors are obtained that give good to excellent fastness properties.

The procedures used in dyeing Saran are relatively simple. Saran contains plasti-

cizers and stabilizers that would be extracted by highly alkaline scouring baths, or by excessive temperatures or time schedules in dyeing.

The conditions to be used in drying Saran are important. The water on Saran is "surface water," and high drying temperatures are not necessary and can be actually harmful. The major portion of the drying should be attained by air flow rather than heat. The air flow should be increased as much as is practical. The temperatures should be kept as low as practical, probably not over 160-180°F., and at these temperatures 15-25 minutes should be sufficient.

Saran staple fibers can be processed on standard textile equipment with slight modifications. Yarns have been produced on the woollen, worsted, jute, modified jute, and the linen systems of spinning. Because of the high denier per filament ratio at present, Saran has not been successfully handled on the cotton system. Most of the Saran yarns have been produced on the woollen system. Here only minor machine adjustments have been necessary.

#### USES

Saran monofilaments have found a wide variety of uses. Typical applications are automobile seat covers, outdoor furniture, shade umbrellas, filter fabrics, insect screens, tobacco shade cloths, and brush bristles.

In the home furnishing field Saran's excellent wear, moth, mildew, and fire resistance, ease of cleaning, and fast colors have led to applications in rugs, carpeting, drapery, and upholstery. Its excellent chemical resistance has led to applications in the filter-cloth field in both yarn and staple form. The high luster and the beautiful lifelike colors of Saran plus its ability to be set or curled led to its application for doll's hair and for wigs.

#### Bibliography for Saran

- (1) Goggin, W. C., and Lowry, R. D., *Ind. Eng. Chem.*, **34**, 327 (1942).
- (2) Matheson, L. A., and Boyer, R. F., *Ind. Eng. Chem.*, **44**, 867 (1952).
- (3) *Modern Plastics* **19**, No. 12, 33 (1942).
- (4) Palmer, J. A., *Modern Plastics*, **22**, 141 (1944).
- (5) Reinhardt, R. C., *Ind. Eng. Chem.*, **35**, 422 (1943).
- (6) U.S. Pat. 2,160,903 (1939), J. H. Reilly and R. M. Wiley (to Dow Chemical Co.).
- (7) U.S. Pat. 2,160,904 (1939), J. H. Reilly and R. M. Wiley (to Dow Chemical Co.).
- (8) U.S. Pat. 2,160,931 (1939), R. M. Wiley (to Dow Chemical Co.).
- (9) U.S. Pats. 2,160,933-5 (1939), R. M. Wiley (to Dow Chemical Co.).
- (10) U.S. Pat. 2,160,939 (1939), R. C. Reinhardt (to Dow Chemical Co.).
- (11) U.S. Pat. 2,160,948 (1939), R. M. Wiley, F. N. Alquist, and H. R. Slagh (to Dow Chemical Co.).
- (12) U.S. Pat. 2,206,022 (1940), E. C. Britton and C. W. Davis (to Dow Chemical Co.).
- (13) U.S. Pat. 2,220,545 (1940), R. C. Reinhardt (to Dow Chemical Co.).
- (14) U.S. Pat. 2,232,933 (1941), R. M. Wiley and J. E. Livak (to Dow Chemical Co.).
- (15) U.S. Pat. 2,233,442 (1941), R. M. Wiley (to Dow Chemical Co.).
- (16) U.S. Pat. 2,235,782 (1941), R. M. Wiley (to Dow Chemical Co.).

L. F. SAMLER AND L. V. JONES

#### POLYESTER FIBERS

Polyester fibers are made from high polymers that are, chemically, condensation products of alcohols and organic acids or of hydroxy acids. Such polymers contain



the ester linkage as part of the macromolecular chain, and not, as in some polyester resins, as part of a side chain on an addition polymer base. Polyester fibers are produced commercially as of 1954 by the Du Pont Company under the trade name Dacron. A similar fiber trade-marked Terylene is in pilot plant production by Imperial Chemical Industries, Ltd., in Great Britain. Both of these fibers are made from polyethylene terephthalate  $\text{HO}[\text{CH}_2\text{CH}_2\text{OOC}_6\text{H}_4\text{COO}]_n\text{CH}_2\text{CH}_2\text{OH}$ , the polycondensation product of ethylene glycol and terephthalic acid.

Dacron polyester fiber is white, and, depending on the amount of delustering pigment added to the polymer, can vary from lustrous and semitranslucent to dull and opaque. Individual fibers are round in cross section, with a smooth surface. Both continuous filament yarn and staple fiber are manufactured. As of 1954, Dacron has been produced only in limited quantities; eventual uses may change as supplies increase (25,31,41), but the chief applications have been in the fields of wearing apparel, household goods, and industrial products. Specific applications include suits, uniforms, slacks, shirts, blouses, sweaters, socks, curtains, linens, sewing thread, conveyor belts and fabrics, ropes, cordage, and fire hose.

The development of Dacron polyester fiber has its origin in the work of W. H. Carothers and his associates, beginning in the late 1920's. In their endeavors to build giant molecules (molecular weights of over 10,000), they first tried polyesters (9). Although they did obtain high molecular weights (18,19,20,21), it was felt that the ester linkages were too susceptible to cleavage for stability, and polymer melting points were too low, so they turned their attentions to mixed polyesters and polyamides, and then to polyamides alone. This work (see *Polyamides*) resulted in the production of nylon, the first wholly synthetic textile fiber.

In the early 1940's, Whinfield and Dickson, of the Calico Printers Association, Ltd., began a study (15) of the effect of molecular symmetry (4) on condensation polymers. By 1941, they had prepared laboratory-scale quantities of polyethylene terephthalate polymer (16) and had found that, from the polymer, fibers could be prepared (17) which were resistant to hydrolysis and had high melting points, as well as being cold-drawable and strong. Further work on this fiber, given the trade-mark Terylene, was delayed by World War II. In 1947 this research was taken over by Imperial Chemical Industries, Ltd., and pilot plant production was begun in 1948.

Meanwhile, Izard and his co-workers, seeking to expand the earlier findings of Carothers, had begun a re-examination of polyesters and had independently duplicated Whinfield and Dickson's discovery of the fiber-forming properties of polyethylene terephthalate. As a result of parallel developments (26,27,32), Du Pont purchased the U.S. patent application and received the subsequently issued patent (24) on polyethylene terephthalate. Dacron polyester fiber (earlier known by the laboratory designation "Fiber V") first became available on an experimental basis in 1950. The first full-scale plant, located in Kinston, N.C., began production in March, 1953.

Three types of Dacron filament fibers and one type of Dacron staple and tow fibers are produced. These are types 5100 and 5500 bright filament yarns, type 5600 semidull filament yarns, and type 5400 semidull staple and tow fibers.

### Physical and Chemical Properties (3,6,10)

Dacron polyester fiber has a density of 1.38 g./ml. at room temperature and melts at approximately 250°C. Since Dacron is thermoplastic, it is possible to heat-set

fabrics made of the fiber in the same manner as fabrics of nylon. Such heat setting is stable to normal washing and ironing treatment. The physical properties of greatest interest are those which are concerned with its use as a textile fiber; they are discussed below.

*Tenacity and Elongation.* Data on the average tenacity, tensile strength, and elongation of recent pilot plant productions of Dacron fibers are listed in Table I. Samples were conditioned at 72% relative humidity and 75°F. and tested on a Suter tester. The data for types 5100, 5500, and 5600 filament yarns were obtained by using yarn samples taken directly from shipping tubes. The data for type 5400 fibers were obtained on dried and conditioned uncrimped tow samples.

TABLE I. Tenacity, Tensile Strength, and Elongation of Dacron.

Fiber	Breaking tenacity, g./denier	Tensile strength, p.s.i.	Breaking elongation, %
Type 5100 (filament yarn)	6.0	About 106,600	12
Type 5500 (filament yarn)	4.8	About 85,000	20
Type 5600 (filament yarn)	4.8	About 85,000	20
Type 5400 (uncrimped tow) <sup>a</sup>	3.8	About 67,000	38

<sup>a</sup> Staple fibers are produced from type 5400 tow.

*Recovery from Stretch.* Some laboratory measurements of recovery from stretch of several samples of experimental continuous filament Dacron yarn with low and high breaking elongations are listed in Tables II, III, and IV.

TABLE II. Recovery from Stretch—Rapid Rate of Loading.

% stretch	Tensile recovery from stretch	
	Low-elongation yarn, % recovery	High-elongation yarn, % recovery
2	100	97
4	100	90
8	90	80

TABLE III. Recovery from Stretch—Intermediate Rate of Loading.<sup>a</sup>

% stretch	Tensile recovery from stretch		Work recovery from stretch	
	Low-elongation yarn, % recovery	High-elongation yarn, % recovery	Low-elongation yarn, % recovery	High-elongation yarn, % recovery
1	100	99	82	85
3	82	82	49	47
5	69	62	35	26

<sup>a</sup> Yarn samples loaded at rate of 10% extension per minute, held 30 seconds after loading, and then unloaded to permit recovery at rate of 10% per minute.

*Stress-Strain Curves.* The initial modulus (resistance to initial stretch) of Dacron polyester fiber is high in comparison with other synthetic fibers. As with most other fibers, the stretch resistance of Dacron is lower at elevated temperatures than at room temperature, but unlike most fibers it is not affected appreciably by moisture or relative humidity conditions.

TABLE IV. Recovery from Stretch—Slow Rate of Loading.<sup>a</sup>

% stretch	Work recovery from stretch		
	Low-elongation yarn		High-elongation yarn
	60% r.h., 70°F., % recovery	Wet, 70°F., % recovery	60% r.h., 70°F., % recovery
0.5	92	92	97
1	71	79	85
2	60	60	54
5	64	—	32

<sup>a</sup> Yarn samples loaded at rate of 1% extension per minute. Samples held in stretched condition 30 seconds and then unloaded to permit recovery at rate of 1% per minute.

Some information on the modulus and other stress-strain characteristics of Dacron fibers at 72% relative humidity and 75°F. may be obtained from stress-strain curves (see Fig. 1). Although curves are shown for types 5100 and 5500 yarns only, type 5600 yarn has about the same stress-strain characteristics as type 5500 yarn. The data for

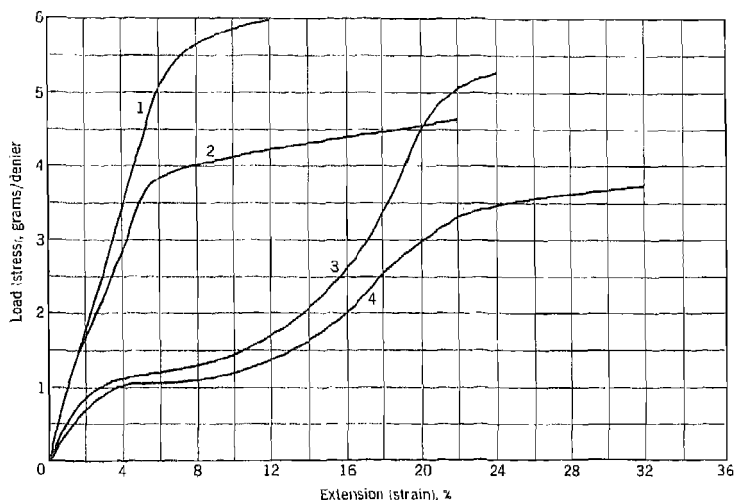


Fig. 1. Stress-strain curves for various types of Dacron polyester fibers. 1, 220-50-5100 yarn; 2, 250-50-5500 yarn; 3, 220-50-5100 yarn; 4, 250-50-5500 yarn. Yarns 1 and 2 were tested immediately after twisting; yarns 3 and 4 were dried and conditioned after boil-off (1 hr. at 212°F.) before testing.

preparing these curves were obtained on an Instron tester at 10% rate of extension per minute, using yarn samples from pilot-plant production. Continuous filament yarns from zero-twist shipping tubes were used, with three turns per inch twist added after removal from tubes.

**Chemical Properties.** Dacron is soluble in the following materials: hot *m*-cresol, trifluoroacetic acid, *o*-chlorophenol, a mixture of seven parts of trichlorophenol and ten parts of phenol (by weight), and a mixture of three parts of phenol and two parts of tetrachloroethane by weight.

Dacron polyester fiber has negligible moisture regain (0.4% at 60% r.h. and 70°F.) and, as Table IV shows, is little affected by the presence of water.

Swelling agents (materials which cause an appreciable increase in fiber cross-sectional area) for Dacron include the following solutions or dispersions in water, all but the first four being dispersed with a synthetic detergent: 2.0% benzoic acid, 2.0% salicylic acid, 2.0% phenol, 2.0% *m*-cresol, 0.5% monochlorobenzene, 0.5% *p*-dichlorobenzene, 0.5% tetrahydronaphthalene, 0.5% methyl benzoate, 0.5% methyl salicylate, 0.3% *o*-phenylphenol, 0.3% *p*-phenylphenol.

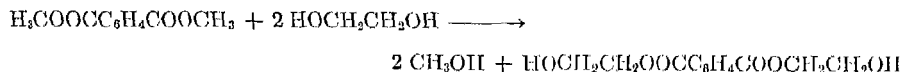
Laboratory tests indicate that most compounds of the following general types have little or no effect on the strength of Dacron polyester fibers under ordinary conditions of exposure: alcohols, bleaching agents, dry-cleaning solvents, halogenated hydrocarbons, hydrocarbons, ketones, soaps and synthetic detergents, water, including sea water, weak acids, and weak alkalis.

Dacron is resistant to most weak acids, even at boiling temperatures, and to moderately strong acids at room temperature. It is disintegrated by concentrated (96%) sulfuric acid. The fiber is resistant to weak alkalis and has moderate resistance to strong alkalis at room temperature but is degraded by strong alkalis at elevated temperatures. Dacron is resistant to oxidizing agents and is not degraded by normal bleaching treatments.

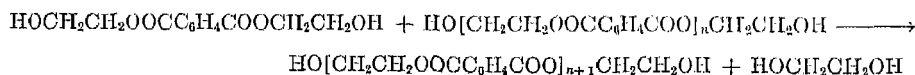
Dyeing (2,10,14) of Dacron polyester fiber requires methods which take into account its low water absorption. While there is considerable similarity in the chemical composition of Dacron and acetate (the  $-\text{COO}-$  group makes up 46% of the weight of Dacron and 41% of the weight of acetate), the compactness of the structure of Dacron is such that the rate of dye diffusion is low. To overcome this difficulty, swelling agents or high-temperature treatment are used. Three techniques are generally practiced: aqueous dyeing at the boil with a carrier (an agent which facilitates dye diffusion; *o*-phenylphenol and benzoic acid are typical carriers); aqueous dyeing at high temperature and elevated pressure, and the Thermosol method, which consists in impregnating the fabric with dispersed dyes and pigments followed by dry heat treatment to effect penetration of the fiber by the dye.

### Manufacture

Polyesters can be obtained by the combination of dibasic organic acids and glycols in a condensation reaction which has water as a by-product, or by other esterification reactions (18,19,20,21,22,23,28,34,35,36). Polyethylene terephthalate can be made in this manner by the reaction of ethylene glycol with terephthalic acid. However, American and British manufacturing experience has shown that the reaction is more readily controlled, and that higher molecular weights are obtained, if the method of ester alcoholysis is used. In this method, dimethyl terephthalate is combined with ethylene glycol, and the lower-boiling alcohol, methanol, is replaced by the higher-boiling glycol. The product is a monomeric diester, bis-(2-hydroxyethyl) terephthalate:



Polymerization of this monomer is brought about by elimination of a molecule of glycol between monomer molecules or partially polymerized chains:



The polymer is formed into fibers by a melt-spinning process similar to that used for nylon. Like nylon, the filaments are drawn after spinning, to increase molecular orientation and fiber strength, although the methods used for drawing may be different from those of nylon technology (29,33,38,39,40).

**Intermediates** (1). Raw materials used in making Dacron polyester fiber are ethylene glycol (see *Glycols*), methanol, and *p*-xylene. The xylene is oxidized to terephthalic acid (see *Phthalic acid*) which is then esterified with methanol and purified to give dimethyl terephthalate (DMT). Very stringent quality requirements are necessary for DMT and ethylene glycol used in fiber making. Traces of impurities can cause either colored or weak yarn and also interfere with the polymerization reaction. Polyvalent metals are particularly harmful, and, for this reason, all processing vessels are made of corrosion-resistant materials (glass, tantalum, or stainless steels).

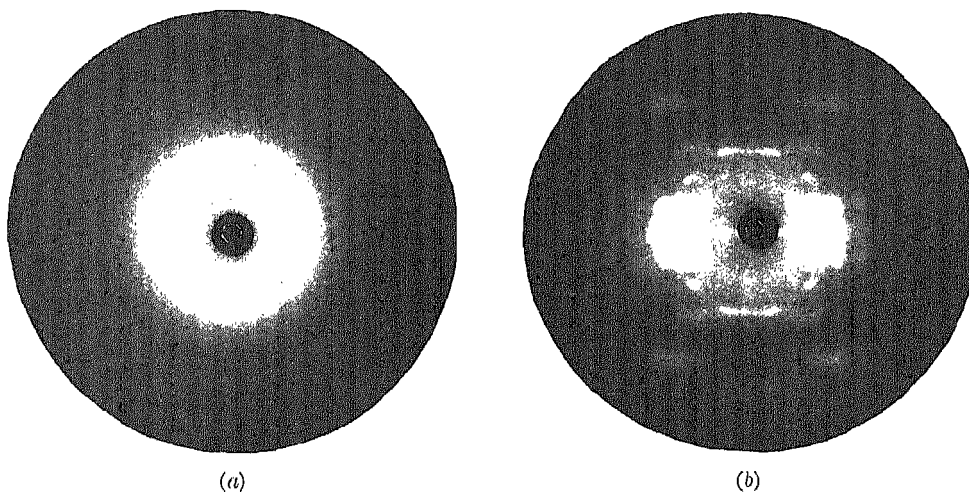


Fig. 2. X-ray diffraction patterns of Dacron polyester fibers. (a) Undrawn fibers; (b) drawn fibers.

**Polymerization.** Formation of polyethylene terephthalate is brought about in two steps, as indicated in the equations above. The first step, alcoholysis, is driven to completion by distilling off the evolved methanol. The second step is chain formation, and here, too, the forward reaction is favored by removing one of the products, ethylene glycol, by distillation, this time under reduced pressure. The polymerization is run at a high temperature to increase the reaction rate and to keep the polymer fluid for ease of handling.

**Spinning.** Melt-spinning of Dacron is generally comparable to melt-spinning of nylon (see *Polyamides*). Melting points are similar although the melt viscosity of polyethylene terephthalate is somewhat higher than that of nylon at the degree of polymerization required for spinning. The molten polymer is forced through a spinneret, solidified by a stream of cross-current air, and then wound on bobbins before being drawn (5,8).

Dacron fibers are made much stronger and more resilient by inducing molecular orientation along the fiber axis (11). This is done by *drawing*, a process of irreversibly elongating the yarn to 2–6 times its original length, and at the same time decreasing the fiber cross-sectional area almost proportionally (drawn yarn is somewhat denser

than undrawn). Figures 2*a* and 2*b* show x-ray patterns of undrawn and drawn Dacron fibers. The pattern for the drawn yarn shows a complex angular symmetry typical of a high degree of orientation. The physical properties of Dacron vary with the degree of drawing—high draw ratios impart a low residual elongation and silklike characteristics, while lower draw ratios give high elongation, resilience, elasticity, and other properties similar to wool. Quantitative measures of these differences have been given in Tables I–IV.

### Economic Aspects

Prices of Dacron polyester fiber yarn in September, 1954, ranged from \$1.60/lb. for staple fiber up to \$3.00/lb. for 40-denier continuous filament yarn.

Since dimethyl terephthalate requirements for the manufacture of Dacron are approximately one pound per pound of finished product, a large-scale demand developed for this intermediate and for its raw material, *p*-xylene. The latter is prepared from petroleum naphthenes by dehydrogenation and isomerization processes, giving a mixture of xylene isomers from which *p*-xylene is separated. Ethylene glycol is in good supply, and the quantity needed for manufacture of Dacron is only a small fraction of the annual production. The same is true of methanol, which does not constitute part of the final fiber product.

### Uses (12,13)

Dacron polyester fiber has found applications in three major categories: wearing apparel, household fabrics, and industrial fabrics and cordage.

In wearing apparel, specific uses of fabrics made with Dacron include outerwear, such as suits, slacks, and topcoats for men and women; men's shirts (both as 100% Dacron and in blends with nylon or cotton) and neckties; and women's blouses, dresses, and lingerie. The resilience and elastic recovery of the staple form make Dacron suitable for knitwear as well. Sweaters, jersey dresses, sport shirts, half hose, and knitting yarn are examples of this application. Continuous filament yarn is used for manufacturing nurses' and waitresses' uniforms, while the staple yarn goes into heavier uniforms, similar to suits and slacks, for air-line personnel, bus drivers, and policemen, where washability and wrinkle resistance are desired.

Household uses of Dacron include curtains, upholstery, slip covers, table linens, and filling for pillows, comforters, and sleeping bags.

Dacron polyester fiber is used in industry for V-belts, conveyor belts and fabrics, covers for flat-work ironing and pressing machines, fire hose, and sailcloth. It is suitable, also, for ropes, nets, and fishing line. Sewing thread of Dacron is used for shoes and in tailoring clothing made from fabrics of synthetic fibers and blends.

### Bibliography

- (1) Bunn, H., *Ind. Eng. Chem.*, **44**, 2128 (1952).
- (2) Carmichael, D. G., *Textile Age*, **15**, 32 (1951).
- (3) Dillon, J. H., *Ind. Eng. Chem.*, **44**, 2115 (1952).
- (4) Edgar, O. B., and Hill, R., *J. Polymer Sci.*, **8**, 1 (1952).
- (5) Heckert, W. W., *J. Chem. Educ.*, **30**, 166 (1953).
- (6) Hill, R., and Walker, E. F., *J. Polymer Sci.*, **3**, 609 (1948).
- (7) Kolb, H. J., and Izard, E. F., *J. Appl. Phys.*, **20**, 564 (1949).
- (8) McFarlane, S. B., *Technology of Synthetic Fibers*, Fairchild, N.Y., 1953.

- (9) Mark, H., and Whitby, G. S., eds., *Collected Papers of Wallace Hume Carothers on High Polymeric Substances* (Vol. I of *High Polymers*), Interscience, N.Y., 1940.
- (10) Maurer, L., and Wechsler, H., *Modern Textiles Mag.*, **34**, 82 (1953).
- (11) Quig, J. B., *Textile Research J.*, **23**, 280 (1953).
- (12) Quig, J. B., and Dennison, R. W., *Ind. Eng. Chem.*, **44**, 2176 (1952).
- (13) Spiro, A. M., *Ind. Eng. Chem.*, **44**, 2151 (1952).
- (14) Turnbull, S. G., Jr., *Am. Dyestuff Repr.*, **41**, 75 (1952).
- (15) Whinfield, J. R., *Nature*, **158**, 930 (1946).
- (16) Whinfield, J. R., *Endeavour*, **11**, 29 (1952).
- (17) Whinfield, J. R., *Textile Research J.*, **23**, 289 (1953).
- (18) U.S. Pat. 1,995,291 (March 26, 1935), W. H. Carothers (to Du Pont).
- (19) U.S. Pat. 2,071,250 (Feb. 16, 1937), W. H. Carothers (to Du Pont).
- (20) U.S. Pat. 2,071,251 (Feb. 16, 1937), W. H. Carothers (to Du Pont).
- (21) U.S. Pat. 2,333,639 (Nov. 9, 1943), R. E. Christ and W. E. Hanford (to Du Pont).
- (22) U.S. Pat. 2,410,073 (Oct. 29, 1946), J. B. Howard (to Bell Laboratories).
- (23) U.S. Pat. 2,423,093 (July 1, 1947), C. J. Froese (to Bell Laboratories).
- (24) U.S. Pat. 2,465,319 (March 29, 1949), J. R. Whinfield and J. T. Dickson (to Du Pont).
- (25) U.S. Pat. 2,512,433 (June 20, 1950), L. Leben (to Imperial Chemical Industries).
- (26) U.S. Pat. 2,518,283 (Aug. 8, 1950), E. F. Casassa (to Du Pont).
- (27) U.S. Pat. 2,534,028 (Dec. 12, 1950), E. F. Izard (to Du Pont).
- (28) U.S. Pat. 2,551,732 (May 8, 1951), J. G. M. Drewitt and J. Lincoln (to Celanese Corp.).
- (29) U.S. Pat. 2,556,295 (June 12, 1951), A. Pace, Jr. (to Du Pont).
- (30) U.S. Pat. 2,558,547 (June 26, 1951), E. W. Ekeley.
- (31) U.S. Pat. 2,571,319 (Oct. 16, 1951), E. Waters and L. Wood (to Imperial Chemical Industries).
- (32) U.S. Pat. 2,578,660 (Dec. 18, 1951), L. A. Auspos and J. B. Dempster (to Du Pont).
- (33) U.S. Pat. 2,578,899 (Dec. 18, 1951), A. Pace, Jr. (to Du Pont).
- (34) U.S. Pat. 2,589,688 (March 18, 1952), P. J. Flory and F. S. Leutner (to Wingfoot Corp.).
- (35) U.S. Pat. 2,594,144 (April 22, 1952), P. J. Flory and F. S. Leutner (to Wingfoot Corp.).
- (36) U.S. Pat. 2,595,343 (May 6, 1952), J. G. M. Drewitt and J. Lincoln (to Celanese Corp.).
- (37) U.S. Pat. 2,597,557 (May 20, 1952), L. E. Amborski (to Du Pont).
- (38) U.S. Pat. 2,604,667 (July 29, 1952), H. H. Hebelers (to Du Pont).
- (39) U.S. Pat. 2,604,689 (July 29, 1952), H. H. Hebelers (to Du Pont).
- (40) U.S. Pat. 2,611,923 (Sept. 30, 1952), H. F. Hume (to Du Pont).
- (41) U.S. Pat. 2,615,784 (Oct. 28, 1952), W. R. McClellan (to Du Pont).

S. A. ROSSMASSLER

### TETRAFLUOROETHYLENE FIBERS

Fiber made from the polymer of tetrafluoroethylene was introduced in experimental quantities by E. I. du Pont de Nemours & Co. in 1954 under the trade-mark Teflon. Other forms of this polymer marketed by du Pont under the same trade-mark are resin finishes, coated glass fabrics and tapes, and wire enamels. See *Resins containing halogens*.

Teflon tetrafluoroethylene fiber retains the unusual properties of the parent polymer of having excellent chemical and heat stability. Chemically, Teflon is affected only by fluorine and chlorine trifluoride at high temperature and pressure, and by molten alkali metals. Temperaturewise, the modulus of the fiber begins to decrease between 212 and 300°F.; the fiber's zero strength temperature—the temperature at which it will support a load of only 0.1 gram per denier without breaking—is 590°F. The upper limits of its useful temperature range are believed to be between 400 and 525°F., depending on the type of application. This combination of high heat stability and chemical inertness makes the fiber useful for industrial applications.

Some of the end uses considered appropriate for Teflon fiber include filter fabrics;

packing for pump and valve shafts; gaskets; laundry textiles for press covers, pads, and roll covers; special conveyors, and beltings; diaphragms for valves; electrical tapes and wire wraps; and special sewing thread. The coating of Teflon yarn with a metallized latex to conduct electric current has also been reported.

The fiber is nonflammable and has excellent electrical properties. It absorbs no water and is highly water-repellent. Its dyeability is poor; although it is tan to brown, as produced, it can be bleached white in a strong oxidizing mineral acid.

The antiadhesive properties of Teflon tetrafluoroethylene resin are carried over into the fiber. The fiber is slippery and few materials stick to it with any degree of adhesion. Its coefficient of friction is the lowest of any fiber known; for boiled-off yarn, the dynamic coefficient of friction is 0.28, the static, 0.20.

On exposure to elevated temperatures, Teflon fiber shrinks moderately. This shrinkage does not continue on further exposure; therefore, fabrics from Teflon may be preshrunk by brief exposure above the intended service temperature.

For 400°F., or possibly higher, fabric operating temperature, the following step-wise procedure (1) has been recommended for fabrics, such as gas filter fabrics and laundry textiles: (1) relaxed boil-off of gray goods, if sized (by rope form in beek, or by stick or book method, or by Henniken machine); (2) relaxed drying (loop dryer); (3) napping lightly or sueding lightly (gas filter fabric) (conventional wire nappers or sand rolls); (4) preshrinking—(a) overfeed pin tenter, at least 500°F., preferably 550°F. or, even better, 600°F.; one minute, 15% overfeed framing at 85% of gray width or (b) completely relaxed on metal belt, one minute at 600°F.

Napping or sueding of continuous filament twill fabric, on the side where the filling floats predominate, yields a fabric that will show minimum back pressure when used as a gas filter. The construction must be adjusted in the loom to produce a fabric which after finishing will have the required gas permeability.

Liquid-filter fabrics in temperature environments of 212°F. or less will not require preshrinking. On the other hand, in the filtration of liquids such as oils, where temperatures are higher, preshrinking may be advisable. In some critical liquid filtrations at moderate temperatures, boil-off at least may be advisable, if the fit of fabric to equipment demands low tolerance.

The heat treatment of fabric of Teflon has been reported as adaptable to an apparatus originally designed to remove size from glass fabrics.

The flex abrasion resistance of Teflon is above that of rayon and Orlon acrylic fiber at room temperature, but below that of nylon and Dacron polyester fiber. However, in many chemical atmospheres or at high temperatures, Teflon is superior in flex abrasion resistance and freedom from brittleness.

TABLE I. Physical Properties of Teflon Tetrafluoroethylene Fiber (Boiled-off).

Denier/filament	6.7
Density	2.3
Tensile strength	
Grams/denier	1.5
P.s.i.	44,200
Elongation, %	24
Initial modulus	
Grams/denier	15
P.s.i.	442,000



The fiber has a round cross section. First experimental production has consisted of 400 denier yarn composed of 60 filaments with one turn of Z twist and mounted on a one-pound cone.

Table I summarizes the physical properties of Teflon tetrafluoroethylene fiber.

Table II shows the properties of Teflon at room temperature after exposure to hot, corrosive liquids. The property changes shown are due entirely to heat relaxation.

TABLE II. Room-Temperature Properties of Teflon Tetrafluoroethylene Fiber after Exposure to Hot, Corrosive Liquids.

Conditions	Tenacity, grams/denier	Elongation, %
Control	1.9	31
Concd. $\text{H}_2\text{SO}_4$ , 5 min. bleaching at 600°F.	1.1	95
Concd. $\text{H}_2\text{SO}_4 + \text{HNO}_3$ , 4 hr. at 320°F.	1.2	65
25% caustic, 4 hr. at 240°F.	1.4	83

Teflon polymer is not toxic. However, when it is heated above 400°F., it gives off toxic gases. Under these conditions, areas where Teflon is being handled should be adequately ventilated and personnel should be warned about the danger in breathing the gases. Care must also be taken to prevent the possibility of accidental inhalation of vapors from Teflon by indirect means. For example, lint from Teflon fiber adhering to carelessly exposed cigarettes would be a health hazard when the cigarettes are smoked.

### Bibliography

- (1) "Teflon" Tetrafluoroethylene Fiber, Bulletin No. 1, issued by DuPont, June 1954, p. 17.

P. M. LEVIN

### GLASS FIBERS

Methods of forming glass fibers were known in the U.S. as early as 1890, and at the Columbian Exposition in 1893 Edmund Drummond Libbey displayed fabrics of relatively coarse glass fibers arranged in bundles and woven together with silk threads. These fabrics were quite impractical since they could not be folded without breaking the filaments.

The manufacture of glass in fibrous form became commercially significant following the development in the United States of high-speed processes that produced a commercially useful product in the period from 1931 to about 1937. Fibrous glass was first produced as a relatively coarse fiber (used for air filtration), then as a somewhat finer wool-type fiber (used predominately for thermal insulation and absorption purposes, see *Insulation, thermal*), and about 1936 as a fiber or filament sufficiently fine to find textile applications. This discussion deals only with the textile type of glass fibers. The principal markets for these products are in electrical applications and in certain types of industrial and decorative textiles—as a reinforcing component for plastics, rubbers, papers, gypsum, etc. See also *Glass*.

The fibrous glass industry in the U.S. has grown in dollar volume from an unknown but probably negligible specialty business in 1930 to approximately \$150,000,000 in 1953, of which it is estimated that textile-type fibers amounted to \$25,000,000.

## Properties

Typical compositions of the three glasses used to form commercial glass textile fibers are shown in Table I; major properties in the massive form are shown in Table II. The low-alkali lime-soda borosilicate is used for electrical and most industrial and decorative fabrics; the soda-lime borosilicate is used for maximum resistance to acid attack, as in filter cloths; the high-lead silicate is used for its x-ray opacity in surgical and some radiation protective applications.

TABLE I. Chemical Compositions of Commercial Glass Textile Fibers.

Type	Composition, wt. %							
	SiO <sub>2</sub>	Al <sub>2</sub> O <sub>3</sub>	CaO	MgO	BaO	Na <sub>2</sub> O	K <sub>2</sub> O	PbO
Low-alkali, lime-soda borosilicate	54.5	14.5	22.0	—	8.5	0.5	—	—
Soda-lime borosilicate	65.0	4.0	14.0	3.0	5.5	8.0	0.5	—
High-lead silicate	34.0	3.0	—	—	—	0.5	3.5	59.0

TABLE II. Properties of Glasses in Massive Form.

Type	Coeff. of expansion $\times 10^{-7}$ per °C. (0–300°C.)	Softening point, °C.	Sp.gr.	$n_D^{20}$	Dielectric properties (23.9°C.)			
					10 <sup>1</sup> cycles		10 <sup>10</sup> cycles	
					Dielect. const.	Power factor	Dielect. const.	Power factor
Low-alkali, lime-soda borosilicate	60	830	2.596	1.548	6.43	0.0011	6.3	0.006
Soda-lime borosilicate	72	750	2.540	1.541	7.46	0.0008	6.9	0.010
High-lead silicate	—	—	4.3	—	—	—	—	—

TABLE III. Comparison of Properties for Low-Alkali, Lime-Soda Borosilicate Glass.

Property	Massive glass	Fiber
Sp.gr. (30°C.)	2.59	2.54
Coeff. of expansion (25–200°C.), per °C.	$60 \times 10^{-7}$	$50 \times 10^{-7}$
Sp. heat (25–100°C.), cal./(gram)(°C.)	0.20	0.19
Refractive index, 550 m $\mu$ at 32°C.	1.552	1.548
Young's modulus of elasticity, p.s.i.	$12 \times 10^6$	$10 \times 10^6$

Certain differences in properties exist between a glass in fiber and massive form which result from the large difference in rate of cooling from the molten state. High-speed attenuation into fibers chills the glass at rates unachievable in sections, so that the glass is far from stabilized at its strain point, and its internal structure is more open with a greater degree of disorder than in annealed glass. Because of this modified structure, the viscosity characteristics of fibers differ from those of annealed glass to a material extent. For commercial fibers, stress release (resulting in permanent set) is not appreciable at temperatures below 200°C. When heated above this temperature, the structure moves toward stabilization and the physical properties toward values obtained for annealed massive glass. Table III indicates the difference in physical properties values for the first glass of Table I in massive and fiber forms.

Of primary interest is the high strength of glass fibers. Breaking strengths of freshly drawn fibers have been measured up to 900,000 p.s.i. and fine fibers of silica

glass, tested in vacuum, have shown strength values approaching  $2 \times 10^6$  p.s.i. Single fibers removed from production strands of the continuous-filament type show tensile strengths ranging from 250,000 to 300,000 p.s.i. It is also established that the breaking strengths of glass rods with especially smooth surfaces are comparable with the values measured for fine fibers, suggesting that the high strength of these fibers results largely from their surfaces being free from flaws of perceptible magnitude.

A currently accepted belief that the strength of glass fibers increases with decreasing diameter was based on the work of Griffith in 1920, which was generally confirmed by Reinkober, Shurkov, Anderegg, Murgatroyd and others. However, Otto (9) concludes that, contrary to current belief, the strength of virgin glass fibers does not depend on diameter. Otto presented evidence that the thermal history of a fiber during formation is the controlling factor and that breaking strengths of fibers produced under nearly identical controlled conditions are identical within experimental limits. This finding holds for the diameter range 0.0002–0.002 in. and suggests that previous investigators, who quite probably were obliged to vary forming conditions to change fiber diameter, mistakenly attributed strength differences to diameter rather than forming conditions.

The high strengths of virgin fibers are not fully realized because glass is scratch-sensitive, and hence in the various manufacturing processes some impairment of theoretical strength is inevitable. The fatigue characteristics of individual glass fibers are less pronounced than for massive glass, and in the form of textile products are further modified by combining them into yarns, and by the coatings used, such as lubricants and sizing materials.

Commercial continuous filament yarns show a tensile strength, when measured by standard procedures (A.S.T.M. D578–52), normally in excess of 6.5 grams/denier, or approximately 210,000 p.s.i., based on the cross-sectional area of the fibers. As far as can be determined, there is no reduction in cross section at break. However, strength is dependent to some degree upon yarn construction and the amount of twist, and when yarns are woven into cloths, the breaking stress for the average warp yarns will be somewhat lower than for the individual yarns. When any glass textile yarn or fabric is intended for stress applications, it should be tested under conditions that approximate those it will see in service.

The electrical properties of fibrous glass products depend in some degree on the volume and surface resistivity and dielectric loss. But in fibrous form the glass serves principally as a support and reinforcement for varnish, resins, or other dielectric materials, which fill the interstices between the yarns. Hence the electrical properties of fibrous glass are determined largely by the particular varnish or resin employed.

The chemical durability of glass fibers is magnified in importance over that of the massive glass by reason of the immensely extended surface area presented by fibers of the diameters used in textile applications. For example, a typical textile fiber having a diameter of  $23 \times 10^{-5}$  in. will have a surface area of approximately 1300 sq.ft. per pound of glass. The first glass shown in Table I has unusually good weathering properties; the second glass has substantially high resistance to acid attack; hence by selection of the correct composition a wide range of surface conditions can be satisfied.

Fibrous glass textiles are made from either staple fiber or continuous filaments made up into a strand of 100, or more often 400, filaments in parallel, lightly held together during subsequent operations with a starch-base sizing. The continuous-filament yarn presents a substantially smooth surface of relatively high sheen; the

staple-fiber yarn has a fuzzy texture. Both types are made in fiber diameters ranging from  $23 \times 10^{-5}$  in. to approximately  $48 \times 10^{-5}$  in.

The individual fibers have extremely smooth surfaces and are substantially cylindrical in shape appearing in cross section as almost perfect circles.

Glass fibers can be readily identified in any fabric by simply burning off or dissolving all organic components of the fabric. The glass fibers are incombustible and will melt but cannot burn. They can generally tolerate up to approximately 1000°F. in service.

The elasticity of glass fibers is unique in that they are perfectly elastic; the stress-strain relationship is a straight line to ultimate fiber strength. Young's modulus for single fibers is approximately  $10 \times 10^6$  p.s.i. Elongation is in the order of approximately 3% in the individual fibers at break. Low-twist yarns show an elongation at the breaking point of 1.7–2.7%; high-twist yarns show 2.2–3.3% elongation. These two characteristics, elasticity and a limited but definite elongation, are highly significant when glass is used as a reinforcement for plastics, resulting in exceptionally high impact strength. Nevertheless these properties also limit the applicability of the fabric where a material of resilient or stretchable nature is required, unless these qualities are derived from yarn construction and type of weave. Other properties of significance are low moisture adsorption and high strength at elevated temperatures. Accurate tests of clean fibers show that there is a gain of less than 0.4% in weight from adsorbed moisture when absolutely dry fibers are exposed to atmospheres of high relative humidity (90–95% r.h.).

The high tensile strength is retained by glass textiles at elevated temperatures. The tensile strength of glass-fiber tapes actually increases somewhat to a maximum at 350°F., declines to original strength at 500°F., and thereafter falls off. The effect is due to cross-bonding by resin-like heat-caramelized starch in the fiber size.

Glass textiles have not been used for clothing applications of any type except certain thermal insulation forms which have been successfully used as interliners for Arctic and military clothing for cold climates. The low stretch, low moisture adsorption, and the great tensile strength are alone enough to preclude satisfactory performance, because the material could not be tailored readily, nor could a knitted fabric like a stocking be drawn over the foot. The glass produces a sleazy, unpleasant feel in contact with the skin and may cause a mechanical irritation due to the broken ends of fibers (see "Health and safety factors").

### Manufacture

Glass batch is formulated with high accuracy, melted in continuous furnaces, and usually formed into glass marbles approximately  $\frac{3}{4}$  in. in diameter. Recent process developments omit the marble stage, the molten glass being formed directly into fibers from special forehearth. The glass marble stage is useful for inspection of the glass to eliminate any imperfections which might subsequently interrupt the forming operation or cause discontinuities in the fibers or filaments.

In the continuous-filament operation, the glass marbles are remelted in small electric furnaces fitted with perforated platinum bushings on the lower face through which the glass flows by gravity. The normal bushing contains 102 or 204 orifices arranged in rows. On starting, operators bunch and draw the coarse filaments downward through an opening in the floor to a high-speed winding device below. This

device operating at a speed of nearly two miles a minute draws the filaments and winds them as a strand upon a tube. The result of this tension is to cause the molten glass to draw down to a fiber very much smaller than the diameter of the aperture through which it originally flowed. By controlling the temperature (and hence the viscosity), the orifice size, and the rate of pull, it is possible to control the fiber diameter precisely.

The staple-fiber process also begins by remelting glass marbles in a small electric furnace with a similar perforated platinum bushing at the bottom through which fine streams of molten glass flow by gravity. The streams are seized by high-pressure jets of steam or air which rapidly stretch them into long but discontinuous fibers. While in flight, a fiber lubricant is sprayed on the fibers, which then pass through a drying flame to remove water. They collect upon a revolving drum as a gossamer-thin web which is immediately drafted off through a rapidly revolving tube and condensed to form a sliver in which most of the fibers lie approximately parallel. The sliver thus formed is immediately wound on a tube or spool.

Subsequent fabrication follows normal textile practices with both types of material. The continuous-filament strand is drawn from the original winding tube on standard spinning frames and given twist; it may then be plied to form a yarn of any desired construction. The staple sliver is twisted and plied into coarse yarns or drafted, twisted, and plied to form fine, high-count yarns.

In both cases, the characteristic self-abrasion of glass on glass is minimized or eliminated in subsequent spinning and weaving operations by coating the filaments or fibers with a sizing or lubricant during the forming operation (2). The lubricants or sizes may be modified for compatibility with various resins used in glass-reinforced plastics, or they may be removed and replaced in subsequent treatments as noted below.

The resulting yarns may also be dyed or given a variety of different finishes according to their ultimate use. Dyeing is accomplished by first coating the filament with an organic film, using Hycar latexes (emulsion of butadiene-acrylonitrile rubber), and then dyeing using Quilon (stearato chromic chloride complex) as a coupling agent. Other techniques employ protein films which are dyed in the conventional manner with standard dyes.

Internally colored glass has been tried for glass textiles but proved unsatisfactory because of the thin section of the glass and the diffusion of light by the multiple surfaces of very fine fibers. A deep blue glass in massive form would produce only a pale blue tint in the final yarn or fabric.

Fabrics woven of glass yarns are also given various aftertreatments or finishes. Heat cleaning is a high-temperature treatment that removes organic material from the fabric. "Coronizing" is a high-temperature heat treatment that removes organic material, releasing the internal stresses of the yarns, which results in setting the weave and gives a limp hand and excellent draping quality to the fabric. The process requires that immediately after the heat treatment the fabric be immersed in a finish of suitable lubricants or other fiber coatings (21).

Other treatments include heat treating to remove the volatile matter in the fiber lubricant and to caramelize the starch constituents of the size, silicone oil treatment to provide a finish suitable for the manufacture of vinyl-coated and rubber-coated fabrics, and acid leaching and refring to convert the glass fibers to 96% silica glass. This process is similar to the 96% silica glass process described in Vol. 7, p. 183. The fabric or yarn is treated with hot hydrochloric acid, which removes substantially all

metallic ions other than silicon which remains in the silica network. At this stage the fibers are submicroscopically porous and have high water-vapor adsorptivity. Drying followed by firing at high temperature collapses and revitrifies the fiber structure to produce a fabric or fiber that has high temperature resistance approximating that of fused quartz (1800°F. service).

### Nomenclature and Standards

Fibrous glass textiles are identified by a designation consisting of three letters, followed by two numeral designations, as ECD 450-4/4, or CSE 25/2. The first letter is either E (glass suitable for electrical purposes), the first glass in Table I, or C (glass resistant to chemical attack), the second glass in Table I. The second letter is either C for continuous filament, or S for staple fiber. The third letter designates the average fiber or filament diameter, and can be D, E, F, or G, for respectively 23, 28, 33, or 38 in.  $\times 10^{-5}$ .

For continuous filament, the first numeral designation is  $\frac{1}{100}$  of the approximate yardage of basic strand (consisting of 100 or more filaments) in one pound. Thus in the examples given, the yardage of strand in one pound would be respectively 45,000 and 25,000. These figures are subject to small twist correction factors, to compensate for contractions due to twist and weight of sizing. The remaining numerals denote, first, the number of strands twisted to make a yarn (a "singles"): the figure following the slant is the number of these yarns that are plied together (twisting in the opposite direction). Thus 4/4 in the example means 4 strands twisted to a yarn and then 4 of these plied together for the final yarn. If the yarns are not plied, then 0 appears as the final figure; thus, 4/0 denotes a yarn made of 4 strands, unplied. (Such a yarn is unbalanced, or "wild," meaning that it has a tendency to untwist.)

For staple, the first numeral is  $\frac{1}{100}$  of the approximate yardage of the basic sliver, and the number following the slant is the number of slivers plied together. Thus 25/2 means 2500 yards of basic sliver per pound (subject to corrections for twist and sizing) and 2 slivers in the finished plied yarn.

### Health and Safety Factors

Fibrous glass has proved to be remarkably free of any health or safety hazard. Since the glass is a silicate rather than silica, there is no potentiality of developing silicosis from the handling of this material in any form (13).

Sulzberger and Baer carried out an experimental investigation of the effects of fibrous glass on animal and human skin (14). They report in part: "All of the reactions observed were of a transitory and superficial nature. The only parts of the reactions which persisted for more than a few days were slight thickening and brownish pigmentation of the skin. The latter were sometimes apparent for several weeks. No reactions or symptoms outside the rubbed skin areas were observed at any time during the experiment."

### Uses

In the electrical applications, fibrous glass continuous-filament strands and fine yarns are used for magnet wire covering, and both continuous-filament and staple-fiber yarns or slivers and tapes are used for the insulation of various types of wires

and cables. Dyed yarns are used as tracer threads for wire coding and manufacturers' brand identification. Braided fibrous glass sleeveings and tubing, either plain, varnished or saturated, are used for the supplementary insulation of lead wires in electrical equipment.

Glass tapes are used in cable construction and to bind and insulate coils in magnetic equipment. They are made in untreated, varnished, mica-backed, and pressure-sensitive adhesive-backed varieties. Glass cords are used in wires and cables as tension members and as a tying or binding cord in electrical equipment such as motors, generators, and transformers. Cloth and sheet insulations, either plain or varnished or in combination with mica, are used as a high-dielectric and high-temperature coil-form insulation, as insulation in slot sections of preformed coils, as layer insulation for air-cooled transformers, and for many similar uses. They are also employed in the formation of laminates and plastic parts for use where a combination of high strength and good dielectric properties is required in the electrical equipment field.

Fibrous glass fabrics are used for the manufacture of marquisette curtains and heavier printed or dyed drapery fabrics. Glass fabrics are used in commercial and industrial applications as pipe wrapping where an incombustible material is required; as the base for a variety of coated fabrics for awnings, tarpaulins, and waterproofing purposes; in the form of open-weave scrim cloth for the reinforcement of bitumens used in waterproofing applications; in the form of plastic-coated yarn for the manufacture of glass insect screening; and in some special high-temperature or chemical applications as a filtering medium.

Fine yarns have also been used as suture thread in surgery, and yarns made of high-lead glass (third glass in Table I) are used as tracer threads in surgical sponges (for post-operative x-ray identification) and in protective clothing fabrics for x-ray operators and other radiation technicians.

Glass yarns and strands are used as unidirectional reinforcement in the formation of rods, including glass fishing rods, and for other unidirectional applications in reinforced plastics. Fabrics are also used extensively in high-strength reinforced plastics where a maximum weight-strength ratio is required. Cloth is also used for the reinforcement of plastics employed to form high-strength automobile bodies and boat hulls, and for the overcoating of existing small boats to provide a permanent waterproofing and nonfouling surface on hulls and decks. Mats and preforms of "chopped" (that is, short length) continuous-filament strands or yarns are used for the low-cost reinforcement of plastics, where the maximum strengths achieved by woven fabrics are not required. Similar strands are used for the reinforcement of certain rubbers, for the manufacture of high-strength gypsum plasterboards, and in parallel or random lay for the reinforcement of high-strength waterproofing and vapor-barrier laminated papers.

Recent developments include the manufacture of all-glass papers using exceedingly fine fibers in the range from  $\frac{1}{2}$  micron to 3 microns in diameter; these papers may be further reinforced with continuous-filament strands of short length from which the individual fibers are largely dispersed in the paper-making process. Such fibers also contribute dimensional stability to pulp papers.

### Bibliography

- (1) Anderegg, F. O., "Strength of Glass Fiber," *Ind. Eng. Chem.*, **31**, 290 (1939).
- (2) Biefeld, L. P., and Philips, T. E., *Am. Dyestuff Repr.*, **41**, 501 (1952).

- (3) "Fiberglas Textile Yarns and Fabrics," *Am. Wool Cotton Repr.*, **56**, No. 23, 9-10 (1942).
- (4) "Glass as a Textile Fiber," *Cotton (Atlanta)*, **106**, No. 7, 78-79 (1942).
- (5) "Glass Fiber for Filter Cloth," *Fibre and Fabric*, **95**, 2987 (1942).
- (6) Griffith, A. A., *Trans. Roy Soc. (London)*, **A221**, 163 (1920).
- (7) Lewison, E. F., "Rayable Gauze as a Factor of Safety in Surgical Operations," *Bull. Am. College Surgeons*, **27**, No. 1, 39-40 (1942).
- (8) Moses, G. L., *Electrical Insulation*, McGraw-Hill, N.Y., 1951.
- (9) Otto, W. H., "The Relationship of Tensile Strength of Glass Fibers to Diameter" (presented at the 56th Annual Meeting of the American Ceramic Soc., Chicago, Ill., April 21, 1954 (Glass Div.)).
- (10) Phillips, C. J., *Glass: The Miracle Maker*, 2nd ed., Pitman, N.Y., 1948.
- (11) Phillips, C. J., *J. Applied Phys.*, **11**, 173 (1940).
- (12) Schols, R. P., and Montjoy, P. S., "Fiberglas Suture Material," *Am. J. Surg.*, **56**, 619-21 (1942).
- (13) Siebert, W. J., *Ind. Med.*, **9**, No. 1, 6 (1942).
- (14) Sonneborn, R. H., *Fiberglas Reinforced Plastics*, Reinhold, N.Y., 1954.
- (15) Sulzberger, M. D., and Baer, R. L., "The Effects of Fiberglas on Animal and Human Skin—Experimental Investigation," *Ind. Med.*, **11**, 482-84 (1942).
- (16) U.S. Pat. 2,132,702 (Oct. 11, 1938), D. C. Simpson (to Owens-Illinois Glass Co.).
- (17) U.S. Pat. 2,133,237 (Oct. 11, 1938), G. Slayter (to Owens-Illinois Glass Co.).
- (18) U.S. Pat. 2,133,238 (Oct. 11, 1938), G. Slayter and J. H. Thomas (to Owens-Illinois Glass Co.).
- (19) U.S. Pat. 2,308,857 (Jan. 19, 1943), U. E. Bowes (to Owens-Corning Fiberglas Corp.).
- (20) U.S. Pat. 2,571,074 (Oct. 9, 1951), R. L. Tiede and Fay V. Tooley (to Owens-Corning Fiberglas Corp.).
- (21) U.S. Pat. 2,686,737 (Aug. 17, 1954), R. F. Cavoselli and R. K. Gagnon (to Owens-Corning Fiberglas Corp.).

J. A. GRANT

## TEXTILE TECHNOLOGY

For simplicity, textile processing can be divided into the following major steps:

1. Carding and combing.
2. Spinning and throwing.
3. Weaving or knitting.
4. Scouring and other cleaning operations.
  - a. Scouring of wool, cotton, and synthetic fibers.
  - b. Carbonizing and milling of wool.
  - c. Degumming of silk.
5. Bleaching.
6. Miscellaneous treatments.
  - a. Mercerization of cotton.
  - b. Creping.
  - c. Heat-setting of nylon.
  - d. Antistatic treatments.
7. Dyeing and printing.
8. Finishing.

The sequence of operations differs in different mills, depending on such factors as the types of fibers used, the kinds of yarn or fabric produced, the age of the mill and its equipment, and the general economics of competition. In this article the discussion is divided into *predyeing operations* and *postdyeing operations*. However, this division is to a large degree arbitrary, and many of the operations can be carried out either before or after dyeing. This article will not discuss textile production at length, since textile fabric production is primarily mechanical rather than chemical.



The chemical steps, such as scouring and bleaching, will be discussed more fully, and the mechanical steps only briefly, to the extent necessary for understanding the chemical processes. An indication of the greater importance of the mechanical operations is that the chemicals used in processing are termed chemical auxiliaries.

Details on the properties, production, etc., of the individual textile fibers, both natural and synthetic, will be found in such articles as: *Cotton; Fibers; Fibers, vegetable; Linen; Polyamides; Rayon and acetate fibers; Silk; Textile fibers, synthetic; Wool*. Additional information on textile processing will be found under *Coated fabrics; Dyes (application); Fire-resistant textiles; Waterproofing*. For testing methods see *Textile testing*.

## PREDYEING OPERATIONS

### Carding and Combing

The purpose of carding is to separate individual fibers, to form them into a nearly parallel position, eliminating tiny lumps and impurities, and finally to produce a perfectly uniform sliver band. The mechanism for doing this is the result of two centuries of machine improvement, and the process is an intricate one. Combing is a continuation of the carding process, its object being the production of an even, compact, finer, smoother yarn by elimination of the shorter fibers. Prior to the actual carding there are several operations that are governed primarily by physical form of the raw material.

Cotton, as supplied to the mill in bales, must first be loosened or opened before it can be carded. Mixtures from several bales are fed into a bale breaker and various succeeding machines, known by such names as the vertical opener, the Buckley beater, and the horizontal opener, which further open the cotton and remove most of the heavy dirt. The picking operation continues the opening and cleaning and forms the cotton into a continuous, fairly uniform sheet known as a "lap." The carding completes the separation of the cotton right down to individual fibers and thus exerts an additional cleaning action.

Wool sorting is the first process which newly purchased, greasy wool undergoes. It is then subjected to a dusting and opening process by a machine that shakes out loose dirt and sand while loosening or opening up the fleece section into individual staples (the individual length of any fiber). Removal of more tenacious dirt and impurities such as grease and dried perspiration necessitates a scouring process that helps speed up the later processes of carding, spinning, and dyeing (see p. 865). After the scoured wool fiber is air-dried, it is subjected to a mechanical or chemical removal of vegetable matter such as burrs, twigs, seeds, leaves, and straw picked up by the sheep in grazing and not removed by the scouring process (see p. 870). The mechanical process utilizes a burr picker, which is really one of the startling operations in carding. Up to this point wool, because of its source and chemical nature, must be handled differently from other natural and synthetic fibers. All kinds of stock are used in production of woolen yarns. The various virgin wools are blended with reworked wools and even cotton, spun rayon, nylon, and other fibers. The various component lots must first be well cleaned, opened, and freed of impurities. The wool must be oiled separately before it is mixed with cotton or other fibers, virtually none of which must be oiled. The mixture of fibers is run through a mixing blender several times and immediately carded to prevent too much oil absorption by the cotton.

The lubrication of wool stock and the union of wool with other fibers preserve the soundness and staple length, help reduce fly and waste in wool carding and spinning, and permit the draft and twist to be inserted more evenly in the yarn. The oil used must not cause or support spontaneous combustion or discolor the wool, must be easily removed by scouring, and must not impair the fiber strength or corrode the machinery.

Lard oil, olive oil, peanut oil, red oil, and numerous mineral-oil-base lubricants are all used and are generally applied as emulsions. In worsted spinning one strength of emulsion is needed for the carding, gilling, and combing processes, while a somewhat lower strength is employed in drawing or preparing the roving. The oil content of most emulsions ranges from 12 to 40% and should be stable for at least 48 hours. Soap formed *in situ* by addition of an alkali to an oil blend containing a fatty acid is widely used as an emulsifier, as are such nonionic emulsifiers as the oil-soluble polyethylene glycol oleates.

An important recent advance in wool processing was the discovery that colloidal silica (a stabilized silica sol) can be used in conjunction with the oils to strike a better balance between lubricative and adhesive characteristics. The oils used in staple fiber processing often serve the dual purpose of acting as lubricants in the carding operation and as adhesives between fibers in the later drawing operations. The colloidal silica makes possible higher production rates through use of higher drafts, and in combination with the lubricating oil results in finer, stronger, loftier, and more uniform yarns from the drawing and spinning processes. When the oils are used alone (in emulsion), it is frequently desirable to warp-size the yarns before weaving, a step often unnecessary when colloidal silica is employed with the oils.

Most of the other natural fibers can be handled by the wool or cotton system, depending on such factors as end use, length of fiber, degree of purification, and intrinsic properties. Minor cellulosic fibers like flax (linen), hemp, jute, ramie, and sisal must first be separated from the useless parts of the plant and any woody matter that may enclose the cellulose fibers. Flax, for example, is subjected to a fermentation process known as retting (see Vol. 8, p. 385). After drying and various mechanical processes for removal of undesirable impurities, the crude fiber is ready for some type of carding, primitive or highly mechanized.

Animal fibers other than wool are of minor importance. Camel hair, angora goat hair, and rabbit hair are typical. They are in many respects similar to wool but differ in appearance and special properties. Where desirable, they may be handled on a wool card. Rabbit and beaver fur are particularly desirable for use in such articles as hats, table covers, bags, pockets, glove linings. For these purposes they need not be carded, but are usually sorted, dusted, and opened like wool, then soaked and scoured, matted (see "Fulling or milling," p. 870), and pressed with moisture and heat to obtain a thick, firmly packed material.

Asbestos (*q.v.*), an inorganic natural fiber having virtually all the fibrous qualities of cotton and silk, may be processed in much the same way as cotton. The best grades can be processed by opening, carding, spinning, plying and weaving, braiding, or molding. The fibers are prepared and carded and combed in such a way that all the fibers lie parallel to one another. Frequently 4-20% cotton is added in the preparatory operation to increase the tensile strength of the material. Chemical auxiliaries of high reactivity obviously should not be used in the processing.

Synthetic and semisynthetic fibers, although produced as continuous filament

yarn, are also cut to perfectly uniform lengths and sizes comparable to those of natural fibers (they are, however, sometimes deliberately cut to varying lengths). This uniformity has made it possible to handle these synthetic fibers on existent cotton and wool equipment, alone or in certain proportions with the natural fiber. Nylon, for example, may require more opening and picking than rayon staple and may be coated with an antistatic agent by the producer. Various fibers may be tinted at a number of positions in the preparatory opening processes for purposes of subsequent identification. In general, the shorter-cut staple synthetic fibers, up to 2 in. in length, are readily handled on cotton cards, but the regular wool card must be used for longer cut fibers. Blends of fibers, such as rayon and wool, require the use of the wool card.

Two main principles govern carding. Carding proper is the opening of the fiber stock through rotating cylinders or rolls covered with card clothing, a fairly thick sheet material through which are pressed many fine, closely spaced, specially bent wires. Two surfaces usually work together, rotating in the same direction, point against point. In the process the fibers are fully opened, separated, and straightened as one surface takes them from the other against mechanical resistance. The stripping principle involves removal or transfer of the carded stock from the cylinder that has performed the carding. The web, a thin film of fibers, is drawn through a tapered tube or funnel and formed into a sliver or band. Thus a 40-in. web of cotton, for example, may be condensed to a round sliver about 1 in. in diameter.

Woolen carding is generally carried out on a three-card system. In this respect it differs from worsted carding and cotton carding which are one-card systems. While the main objective of worsted and cotton carding is to lay the fibers parallel to each other, no such attempt is made in woolen carding. The fibers in woolen yarn, like those in most nonwoven fabrics, lie in every direction, whereas in a worsted yarn or combed cotton yarn they lie virtually parallel. The three successive cards of the wool system are similar in construction and action and differ only in the fineness of the card clothing and type of delivery of product, the sliver form from the first card being finally delivered in roving or roping form ready for spinning.

*Drawing* (drafting) and *roving* processes, intermediate steps between carding and spinning on all but the woolen system, convert the sliver into roving small enough to be spun conveniently into a fine, even yarn on the spinning machine. In all drawing operations the straightening and parallelization of the fibers is continued. The action is obtained by using several pairs of rolls running at different speeds and by doubling as many as six slivers to make one. In worsted drawing, the Bradford or English system employs a twist and operates with oiled tops, whereas the French or continental system controls without twist and uses dry combed tops. Between five and ten operations are required to reduce the top slivers to the necessary thickness and uniformity of a roving suitable for spinning a satisfactory yarn.

### Spinning

The process of drawing and twisting fibers together to produce a thread or yarn has long been applied to the natural fibers. This mechanical operation is distinct from the chemical process of spinning rayon and other synthetic fibers and the spinning of silk by the silkworm. The purpose of textile spinning of wool, cotton, and cut staple fibers is to reduce the roving to the required size of a single yarn and to insert a suitable amount of twist for the desired end use. The three main classes of yarns are warp,

filling, and knitting yarns. The most widely used production processes are the woolen, Bradford, French, and American systems, each of which imparts a different characteristic to the spun yarns.

Woolen yarn is made from relatively short fiber on a rather abbreviated system. The yarn has a rather rough, fuzzy appearance and less strength than worsted yarns, as the fibers are only partially parallel. The woolen system is very versatile in the variety of fibers that can be used; all the new synthetics can be spun on this system, with or without wool being present. It is a low-cost system because of the few operations and because of its use of short, and hence often inexpensive, fibers. The French system lies at the other extreme because of the higher number of operations and the fine quality of yarns produced. Unlike any other system, French yarn is spun from roving that has no twist. Yet it uses more short fibers (in a blend that averages about 3 in. in length) than other systems except the woolen system. The Bradford system uses longer fibers than any other and employs twist for control in a series of five to seven operations. The American system has fewer operations than the French or Bradford, mainly because the fibers are drafted about twice as rapidly in the roving and spinning.

There are three essential steps in spinning any staple fiber, regardless of whether a mule or a continuous spinner is used. (1) *drafting*, or final drawing out by rolls similar to those used in roving; (2) *twisting*, or insertion of twist, after the yarn strand has been reduced to its required size; and (3) *winding* of the yarn into a suitable package for further use. Drafting delivers a longer, slimmer yarn than that fed to the first roller or spindle. Twisting imparts strength to the yarn.

Regardless of the method of spinning, the drafting is done by rollers and the resultant yarns are longer but smaller in cross section than the roving prior to drawing. Pin drafters have now been adapted to most systems as pin control usually requires fewer operations than roller control. The twist is produced by revolving one end of the strand and holding the other. To obtain strong yarns, considerable twist must be imparted, since twist condenses the loose ribbon of yarn fibers to a compact mass. The greater the twist, up to a point, the harder is the yarn, the optimum being critical in many cases. Twist also shortens the yarn, increases the weight per yard, and helps make possible the creping operation to which many fabrics are subjected (see p. 876).

Warp yarns, which run lengthwise in a cloth, usually have a relatively high twist and maximum strength, partly the result of using long and good-quality fibers. Filling yarns, which run crosswise in a woven fabric at right angles to the warp threads, usually are given less twist. This helps avoid formation of kinks in weaving and gives body and softness to such fabrics. Knitting yarns have even less twist than filling yarns.

Occasionally a twist-setting operation is necessary when tension is released, in order to reduce the "liveliness" of the newly spun yarns and to prevent snarling, kinking, and untwisting in weaving or knitting. Steam boxes, water sprays, steeping systems, or water vapor equipment is employed to solve this problem.

**Throwing of yarn** is a term which may be broadly defined as the preparation of "raw" continuous filament yarn like silk and synthetic fibers for use in the manufacture of a fabric. Raw yarn may be defined as one or more parallel continuous filaments so arranged by the prime producer as to comprise one continuous thread of known size or standard. Most synthetic yarns are delivered on cones by the yarn producers. If no additional twist or coloring or tinting of the yarn is needed, the yarns can be

used directly in the high-speed cone creel in warping. Otherwise the coned yarn must be reeled into skeins for dyeing or twisting.

*Coning* is essentially a transfer operation. It is not only used for repackaging yarns from bobbins, cakes, or spools supplied by the producer, but also as means of applying finishes to yarns by the throwster. Coning machines are often equipped with a so-called "oiling" attachment consisting of a trough and emulsion roll set-up. The coning oil should supply surface lubricity and antistatic qualities; be resistant to oxidation, rancidity, and resinification over a long period of time; be easily scoured from the yarn and fabric; and be practical to apply during coning. As with the natural fibers, temperature and relative humidity must be controlled in rooms where yarn is moving rapidly through machines and under tension.

In general, all sized yarns are oiled during coning. Various types and viscosities of oil are used, the percentage applied varying with the type of oil and end usage of the yarn. Frequently a paraffin-base mineral oil emulsified O/W with a nonionic emulsifier forms the base. It may also contain a rust inhibitor, an antistatic agent, an antioxidant, and even an antifoaming agent. What should be included is a highly controversial matter. Cationic finishing agents are particularly effective on glass yarns, which, though possessing extremely high tensile strength, are readily cut by one another. The cationic agent imparts high lubricity and hence lowers friction, so the amount used on glass must be kept at a minimum lest the yarn be stripped from the cone.

Skein reeling is employed in preparing low-twist filament and spun yarns for skein dyeing and skein sizing. Originally, the machines used for reeling silk were adapted for synthetic yarns, but in 1939 a new skein reeler was developed that requires only one operator instead of three classes of operators. Other rewinding operations are known as copping, quilling, or filling winding, the object being to prepare filling yarns for weaving by winding them into paper cops, quills, wooden bobbins, or special spools to fit the weaving shuttle.

The throwing process has as its objectives the application of a lubricant, size, or other yarn treatment, combining two or more yarns to form one of heavier weight or for special effects, adding twist to yarns, and putting the thrown yarn into a suitable package for weaving or knitting. The yarn producer may insert a low twist as part of his process, but the throwster must insert high twist, if desired, or otherwise prepare the yarn for special effects or modifications. Thus high twist is needed in hosiery leg yarn to increase resistance to snagging and abrasion, and to give permanent dullness, good fitting properties, and sheerness to the finished product. Thrown yarn is also used in tricot knitting and for weaving purposes.

Single-end sizing, as used on nylon, Vinyon, Dacron, Orlon, and other synthetic yarns with which soaking is impractical, may be carried out by throwster, knitter, or weaver. An example of size formulation is the original DuPont formula "PM-90" for nylon, which consists of about 8% polyvinyl alcohol, 1.6% boric acid and water. Although this formula or its modifications serve for hosiery yarn, a water solution of polyacrylic acid is preferred for use on nylon yarns for tricot knitting and weaving. The size is applied by contact between the yarn and a roller revolving in the size trough and is generally added after the twisting operation.

Two basic methods of inserting twist are used on synthetic filament yarns: down-twisting and up-twisting. The down-twisting machine is used for plying or combining two or more ends of (already twisted) yarns while inserting a small number

of turns of twist in the ply. The ply is twisted in the opposite direction to the yarn to prevent a tendency to unravel. The up-twisting method is faster and is used solely to insert twist into yarn. It is convenient to use the terms Z and S twist to indicate the direction of twist and the inclination of fibers in the yarns. If a yarn with Z twist is held vertically, the fibers are seen to lie in the direction of the slanting line in the letter Z; the S twist is in the opposite direction.

### Weaving

The process of weaving transforms yarn into cloth. It involves interlacing the warp and filling threads with each other in a loom. Spooling, rewinding, coning, throwing, and warping are preparatory processes that combine numerous short threads into fewer continuous ends. These are then collected on a beamer that brings all ends into the same horizontal plane in the form of a sheet with hundreds of yarns lying side by side, equally spaced.

At this stage chemical auxiliaries begin to play a major part in textile processing. Virtually all types of warp yarns are *sized*, or "slashed," in order to increase weave room production, and to provide the desired handle or feel and weight. Warp slashing lays the surface fibers of the yarn, making it more compact, smoother, and stronger. With the development of various new filament and spun yarns and particularly of finer deniers and new synthetics of different natures and properties, it has become a complicated problem to get best results at minimum cost. The two major categories are the silk system and the cotton or rayon system, the latter being used most extensively.

Starches, gums, gelatin, softeners, penetrants, preservatives, and occasionally inert loading agents are the basic chemical materials used in formulating warp sizes. Every textile mill has its own ideas about size formulations, some using traditional, proven formulas and others using revolutionary and simplified formulas justified by more modern equipment. The amount of size pick-up required for good weaving and the ratio of the film-forming component to softener are debatable. Some size formulations developed in Europe include inert loading agents such as china clay or talc. Economics naturally plays a part, corn and tapioca starches competing for a market once held almost exclusively by wheat starch and animal glues.

The adhesive, film-forming starches, gums, and glues are at present the most economical base materials for a size, although synthetic resins are competitive. The most important starches used for sizing include cornstarch, thin-boiling cornstarch, chlorinated cornstarch, potato starch, tapioca starch, and sago flour. Natural gums, such as tragacanth, locust bean, and karaya, are frequently added to starch sizes to increase the binding power, water absorption, and flexibility. Animal glue and gelatin are sometimes used to modify starch formulations further, and gelatin is preferred to starch as the base ingredient in sizing rayon filament yarns. Casein, another protein size, competes principally with glue and gelatin.

Starches, gums, and glues that work well on the natural, hydrophilic fibers are not suitable for use on nylon and some of the other hydrophobic fibers. Polymethacrylic acid, sodium carboxymethyl cellulose, and polyvinyl alcohol are generally preferred. The 25% active polyacrylic acid is particularly effective as an adhesive ingredient for nylon warp size compositions. A polyvinyl alcohol composition is widely used on nylon hosiery yarn, while both polyvinyl alcohol and polyacrylic acid are used in sizes for nylon tricot knitting yarns. The use of air conditioning in weaving rooms

of many modern mills has a number of advantages, not only as a means of helping control static problems, but also in controlling such size compound properties as adhesion, film strength and thickness, and uniformity of application.

*Softeners* are used to impart pliability and flexibility to the starch or gelatin film and to provide lubrication to the slashed yarn as it passes through the reeds, heddles, and harnesses of the loom. Tallow and sulfonated tallow have long been favorites, especially for cotton yarns, but numerous other oils, fats, and waxes such as coconut oil, castor oil, stearin, paraffin, and various synthetic oils and fats are often used in size compounds. Sulfonated coconut oil is used extensively with gelatin for sizing filament yarns, while mineral-oil-base lubricants are frequently preferred for cuprammonium yarns. Sulfated olive-cottonseed oil mixtures are used with rayon and acetate, while synthetic materials like the polyoxyalkylene stearates (polyethylene glycol stearates) are advocated as antigelling agents, emulsifiers, and assistant lubricants on the theory that water is the real plasticizer for starch. Since excessive fat content detracts from adhesiveness and weakens and embrittles the resulting film on the yarn, the need for careful formulation of the size is evident. Gelatin and other protein warp sizes for rayon usually require a polyol such as glycerol, sorbitol, or diethylene glycol as a softener and humectant. Ethylene glycol is used in a similar manner in the polyacrylic type of nylon warp size.

Among the minor ingredients used in formulation are the antiseptics or preservatives, defoamers, enzymes, and penetrants or wetting-out agents. Since the major ingredients are ideal foods for all kinds of mold, mildew, and bacteria, it is necessary to add mildew preventives or antiseptics such as the various organic and inorganic chlorides, pentachlorophenol, 2,2'-methylenebis(4-chlorophenol), salicylanilide, copper sulfate, copper 8-quinolinolate, and sodium fluosilicate. Usually cresylic acid is employed as a preservative for gelatin (about 1% of the weight of the gelatin). Defoamers such as the high-molecular-weight alcohols are sometimes added to overcome frothing in the size box (see *Foams*). Enzymes are used in starch sizes to thin the mix and thus give high solids content with lower viscosity and improved penetrating properties. The penetrant is usually a wetting agent (see *Surface-active agents*) which cuts through the natural or inherent finish on the yarn and allows it to wet quicker. Different yarns naturally have different size requirements, spun-dyed acetate needing more penetrant and more size than most fibers, for example, and viscose rayon needing no penetrant.

In preparing a size, a fixed ratio of softener to gum to starch that has proved satisfactory for a given set of operating conditions must be maintained to avoid defective warps. If the warp is too soft, the size content is increased. If the warp is too hard or stiff, the amount of softener is increased. Other important factors are variations in cooking time, temperatures of storage tanks and size boxes, variations in liquor level in the size box, and the condition of raw materials. Most important is the fact that the size must be easily removed in the scouring prior to dyeing.

The size is applied by immersing the yarns under tension in the size baths, squeezing out the excess, and then drying in a steam dresser or dryer over rolls or heated cylinders or cans, or in a hot air chamber. The number of yarns sized at one time (known as the sheet) is determined by the construction of the fabric to be woven. Warp-sizing equipment for filament rayon yarns is similar to conventional cotton slashers, but the equipment is of lighter construction and the moving parts must be well synchronized to prevent excessive stretch or rupturing of the rayon filaments.

It is generally customary to refer to sized continuous filament yarns as thrown yarn. Basically, the throwing process has as its purposes the application of a lubricant, size, or other yarn treatment, the combining of two or more yarns to form one of heavier weight, adding twist to the yarns, and packaging for use by the fabric manufacturer. The hosiery industry is a traditional customer of thrown yarn, and most thrown yarn is used for knitting rather than weaving.

Weaving is a continuous process, but it involves many separate and dissimilar motions and parts, acting intermittently and out of apparent relation to each other when first observed. The beam or roll containing the yarn sheet after it has been sized and dried rotates against friction, feeding the warp yarns under tension through warp-stop-motion drop wires which are provided for each individual warp yarn. The yarns then pass over and under lease rods, through heddle eyes located on the harness frames, and are thus separated into two sets of yarns. One set passes through even-numbered harnesses and heddles, and the other through odd-numbered heddles and harnesses, so that a separation of the harnesses with their heddles creates an opening in the yarn sheet called the shed. The filling yarn is placed in a shuttle on a bobbin and allowed to unravel as the shuttle moves through the shed from one side of the loom to the other. By a series of intricate mechanical devices the yarns are interlaced with each other at right angles to form a fabric. The many variations on the basic principle make possible the composition of many different types of fabric surfaces and fabric strengths.

### Knitting

The process of making fabric by forming loops of yarn and drawing other new loops through those previously formed produces the knitted fabric structure. Machine knitting requires a multiplicity of needles, needle holders, and yarn feeds. The order of interlooping, the way in which the loops are formed, and the types of needles and yarns used determine the type of fabric produced. An important feature is the resultant ability of the fabric to stretch in any direction. Thus garments like sweaters, bathing suits, underwear, and hosiery are knitted.

There are two basic types of knitted fabrics: warp-knit and weft-knit. In warp-knitting a thousand or more yarns feed into the machine at one time, each with its own needle and all forming their loops upon the needles at the same time. It is essentially a system for producing a wide fabric having more or less straight edges and great yardage. Only minor changes can be made once the warp is set up. Tricot, milanese, raschel, and "simplex" fabrics are examples of the warp-knit type. In weft-knitting the yarn is fed into the machine directly from a cone, spool, or other package in such a manner that the yarn is interlooped through a row of loops previously made and lying across the width of the fabric. The yarn may enter from one or more feeds so that one or more rows of loops (courses) can be knitted into the fabric at one time. All hosiery, most sweaters, bathing suits, and knitted outer wear are made of weft-knit fabrics.

In the early days of rayon development, 300-denier and heavier rayon yarns were used for knitting and were first soaked in neatsfoot oil and emulsions of such oils. Today the throwster uses emulsions made of gelatin and emulsifiable oils, or a solvent type of soaking that is generally based on a wax in Stoddard solvent (naphtha) medium (see Vol. 10, p. 167). A typical wax is "Avconit," a synthetic polyethylene



glycol derivative of a sorbitol ester. Such products can function as lubricants, coning oils, and knitting sizes.

### Nonwoven Fabrics

Mention may be made of the nonwoven fabrics. These are essentially a post-World War II development, made possible by synthetic latexes, resins, and celluloses. The manufacturing process is unique in that spinning and weaving, as well as drawing and combing into rovings, are completely eliminated. Instead, webs of fibers come off the machine in a wide sheet with random distribution of fibers. Thus the material has equal strength in all directions. In a few cases, the individual fibers are allowed to run in parallel direction or at right angles like woven yarns, but the biggest trend is toward randomization.

The fibers in the web are bonded together in various ways to form the finished fabric. One method is to mix in the web a proportion of thermoplastic fibers such as Vinylon or plasticized cellulose acetate. When the web is subjected to heat and pressure, these soften and serve as a bonding medium. Another method is to impregnate the web with liquid bonding solutions or emulsions. These binders include the polyvinyl acetate emulsions, polyvinyl alcohols, vinyl chloride copolymers, vinylidene chloride copolymers, acrylic ester, and acrylonitrile copolymers. Plasticizers (*q.v.*) like dioctyl phthalate and alkyl aryl phosphate types are widely used. The end use is important in determining which of the many available types of fibers, fiber-processing methods, and bonding agents will be employed. In general, they offer several qualities unobtainable in most conventional fabrics, such as high porosity, absence of raveling, uniform structure, smooth surface, high absorbency, and, in some types, wet strength, stiffness or softness, cling, and heat sealability.

### Scouring and Other Cleaning Operations

A number of chemical treatments are required at various stages in the formation of yarns and fabrics. The lubricants and film-forming sizes employed in the mechanical operations of forming a yarn and fabric have already been described. Probably even more fundamental is the need for removing all extraneous matter from the fabric, or "gray goods," to secure even dyeing with optimal brilliance. The chemical predyeing treatments include such operations as degreasing, desizing, scouring, steeping, carbonizing, mercerizing, and bleaching. The order and number of such operations will differ for different fibers and even for one kind of fiber, depending on a number of factors. Thus raw wool is scoured while still in the loose state, in contradistinction to cotton and other fibers. Cotton is usually mercerized, but not other fibers. Bleaching of synthetic fibers and yarns is rarely necessary, since they are already bleached in the original process of manufacture.

**Wool Scouring.** As raw wool fiber contains a far higher percentage of impurities than any other major fiber, wool (*q.v.*) must be scoured even before it is carded, while it is in the "loose" state. The amount of impurities varies from 20 to 70%, consisting of fatty material (wool grease (*q.v.*)), suint (dried salts which are derived from various gland extracts other than those of the sebaceous glands), particles of dry grass and straw, thistles, burrs, seeds, dust, dried earth, excrement, as well as tar and paints derived from cattle dips and identification marks. The grease or wool fat contains

fatty acids, wax alcohols, waxy acids, and fatty esters, while the suint contains potassium, sodium, and ammonium carbonate, all fatty acids from acetic to caprylic, stearic and cerotic acids, oxalic, succinic, and other dibasic acids, together with glycine, leucine, tyrosine, and some potassium phenol sulfonate. In the scouring of raw wool there is a weight loss of 20–70%, and of the material removed in this manner about 40% consists of natural fatty matter. Hence the recovery of the wool fat in the effluent from the washbowls leads to a rich source of organic materials.

While soap and hot water are excellent cleaning materials in most cases, wool is very sensitive to both alkali and temperature. Also, any mechanical agitation in the wet state must be kept to a minimum to avoid felting of the material. Emulsion scouring with soap solutions or synthetic detergents at 55°C. or lower is by far the commonest method. Other possible methods for purifying loose wool include suint scouring, solvent extraction, and freezing. In freezing, the wool is exposed to a low temperature so that the grease becomes hard and brittle. This hardened grease can then be removed (along with occluded dirt) by brushing and agitation of the wool.

*Emulsion scouring* of raw wool is continuous, the wool being passed slowly through several vats called "bowls" which contain soap, alkali, or detergents dissolved in water. As a wide generalization, about 2–4% soap and 2% sodium carbonate, based on weight of wool, are used, although formulations vary considerably. The wool is passed along from one bowl to another by mechanical rakes and is squeezed gently between rollers en route. Generally driers are located at the end of the scouring train so that dried wool of the proper moisture content is delivered continuously. The number of bowls in the train varies from three to six, the first generally containing only warm water for removal of the soluble salts. In the second bowl alkali alone or a soap and alkali may be added, most of the fat and dirt being removed here. The third bowl may contain a small amount of soap or synthetic detergent, but only in a three-bowl system will it consist of a warm water rinse. Sometimes a continuous countercurrent flow of liquor from the fourth and fifth bowls is run back to the first bowl, the alkali and soap additions being made only at the second and third bowls.

Neutral scouring with synthetic detergents is necessary for certain wools, such as some of the New Zealand quality wools, which become stained red with alkali. Limed wools, obtained by painting the skin (after removal from the animal) with a cream of slaked lime a day before pulling the wool, may be subjected to neutral scouring to avoid the extra steps involving neutralization of the lime with hydrochloric acid.

Potash-olive oil soaps are frequently considered best for scouring, but a soda soap from olein is a satisfactory substitute in many mills. Among the synthetic detergents, the most widely used are the fatty alcohol sulfates, Igepon T, the alkylated arene-sulfonates, and nonionics such as polyglycol ethers. The nonionic agents can even be used for scouring in the acid solution, although acid scouring of raw wool is unnecessary in most cases, since the presence of free fatty acids, readily saponifiable fatty esters, and natural alkali salts in the grease and suint forms soaps at no extra cost. Soap or detergent and alkali are added to the scouring bath chiefly to replace the naturally formed soaps that are removed in the washing process. Actually the alkali is preferentially absorbed to a degree from the hydrolyzed soaps by the purified wool itself and the wool grease is frequently acidic, so the washing process consumes soap and alkalies in various ways. The process is called emulsion scouring because the primary objective is to emulsify the wool grease into a relatively stable emulsion and to suspend the dirt. Fortunately, some of the grease is self-emulsifying and soap is an

excellent emulsifier. Since the wool grease has considerable value as a commercial product and generally cannot be dumped into sewers or streams because of its physical nature and odor, it is often economical to recover it for sale. Recovery methods include acid-cracking and centrifugal separation.

*Suint scouring* generally operates in five stages: (1) de-suinting, (2) grease removal, (3) rinsing, (4) soaping, and (5) rinsing. It makes use of the clarified wool suint (potassium salts primarily) in what might be described as a natural emulsion process. Suint liquors vary from a pH of 5.5 to 8.4 (that is, not far from neutrality), and temperatures up to 70°C. may therefore be safely employed. Addition of alkalis is sometimes practiced, as is the addition of sodium hexametaphosphate (see Vol. 10, p. 418) (for removal of undesirable metallic soaps) and, in the rinse bowls, of surface-active agents that possess good wetting and high dispersing powers, such as the detergents mentioned above.

*Solvent scouring* with gasoline, carbon tetrachloride, or solvent naphtha in large kiers, in the absence of air, has both advantages and drawbacks. The extracted wool still contains suint that must be removed by water washing, but the method gives wool of excellent quality and eliminates dangers of alkali damage and felting. The freezing process is less effective in removing all the grease and dirt, but as a partial cleansing process it also yields excellent wool because the scouring that must follow can be milder.

*Yarn scouring* of wool is generally carried out with the wool in hank form, the object being to remove the oil that has been added to assist in the spinning operations. It must be done for yarns which are dyed in yarn form for the production of colored-woven fabrics. Large-scale scouring in hank form may be carried out by a series of three or four bowls, each fitted with a powerful squeezing press. Soap and soda ash may be used, or soda ash alone if the lubricant contains free oleic acid, while a self-emulsifying lubricant may require neither, only water and agitation.

Fabrics are generally woven or knitted from unscoured yarn, except as just noted. Most piece goods contain spinning oils and size which are removed by scouring either in rope-form or in open-width. Hosiery is usually scoured in the stocks or in the tomtom machine (a tub-scouring machine). The rope-washing machine, or dolly, is a very versatile piece of equipment that may be used for many different fabrics. It consists of a pair of squeeze rollers below which is situated a small trough to receive the dirty liquor, and the whole is surrounded by a larger trough to contain the detergent solution. The larger trough is equipped to separate the various pieces of cloth which are being scoured. The open-width or broad washing machine is rather similar in design. Wash-wheels or laundry wheels can also be used.

Decision on the proper method to use in scouring a wool fabric is governed by (1) the type of fabric, (2) the probable requirements for subsequent finishes, and (3) the nature and amount of oil in the fabric. The natural grease has undoubtedly been removed during scouring of the raw fiber, so the problem is removal of size and spinning oils. In general, worsteds contain 2-5% oil on the weight of wool, olive oil or neutral oil with a little free olein being commonly employed. Woolens are apt to contain 8-12% of an olein preparation consisting chiefly of crude oleic acid, with small amounts of mineral oil in some cases. Low-grade woolens usually contain 15-25% of a low-grade olein, a substantial part of which is mineral oil. Hence soap is generally used on worsteds, sodium carbonate on woolens, and sodium carbonate plus soap on low-grade woolens. Fuller's earth (see Vol. 4, p. 49) is occasionally used at the low

end of the trade as a mild scouring agent for fabrics, and even for milling in the grease where a mild fulling is also required.

Contamination of wool by paint, tar, and insoluble fluids used in branding sheep or in various cattle dips often demands special treatment. Where possible, the encrusted, dried material is clipped by hand by the wool sorter. These "paint clips" are usually depainted by a special solvent treatment, after which they are used in very cheap fabrics. Often they escape clipping and must be removed, if possible, in fulling or scouring operations. Solvents such as bis(2-chloroethyl) ether, bis(2-chloroisopropyl) ether, ethylene dichloride, *o*-dichlorobenzene, tetrachloroethylene, and trichloroethylene are often added to the soap solution. Sulfated castor, corn, and red oils are sometimes used in combination with pine oil, xylene, cresylic acid, and other solvents. A number of such additive compounds are sold under trade names. The solvent scouring process is an alternative method, and the cleaning up of spots that may have escaped the scouring operation is a final method. Spotting agents are usually dry-cleaning solvents such as those mentioned above, or proprietary mixtures based on such solvents, and a wetting or penetrating agent.

Lather is normally considered essential to good scouring of fabric. Whether the lather itself actually helps or is merely an indication of sufficient soap being present, it is known that clean wool is not obtained without sufficient lather if scouring is done with water. Copious lather in itself is not a sufficient criterion; it must be a permanent type that lasts in the absence of agitation. Sometimes solvents like carbon tetrachloride or methyleyclohexanol (see Vol. 4, p. 770) are added to help remove unsaponifiable matter, while auxiliaries like Igepon T are used to help prevent setting of the grease on worsteds during the preliminary crabbing operation (treatment by hot water or steam or both while on rollers).

**Cotton.** More cotton (*q.v.*) is scoured than any other textile material. Fortunately, cotton and most fibers present less of a scouring problem than do wool and wool unions. The impurities associated with cotton cellulose are waxes, proteins, mineral matter, and natural coloring material. Most of the adherent dust, dirt, pieces of leaf, and seed is removed by mechanical operations prior to sizing and weaving. The waxes actually assist the spinning operation, serving as lubricants, but their water repellency makes them a hindrance in dyeing and bleaching. The other impurities also interfere to a lesser degree.

Various processes are used in removing the impurities, the major steps today involving steeping, scouring, and bleaching, with the mercerizing process sometimes making scouring unnecessary. Many cotton cloths which are valued for their sheer or smooth appearance are first subjected to singeing to burn off the projecting fuzz of cotton hairs. Singeing may be accomplished by passing the goods at high speed over heated surfaces or open gas flames. Removal of the sizing material, chiefly starch, follows the singeing operation. Steeping in warm water for 12–24 hours, the "rot-steeping" method, has been largely supplanted by use of 0.5–1% sulfuric acid or a malt enzyme solution (see Vol. 5, p. 757). While malt extract has been employed for many years, bacterial enzymes such as Rapidase appear to have certain advantages for desizing. Use of the appropriate enzyme is more effective and economic than use of inorganic acids and alkalies. If proper care is taken, it is also much safer.

Cotton is usually scoured in kiers, cylindrical iron vessels holding from  $\frac{1}{4}$  to 5 tons of cloth, in which hot alkaline liquors are circulated under 10–30 lb. pressure. The cotton is usually washed before kiering to remove water-soluble impurities and is impreg-

nated with the scouring liquor before reaching the kiers. The scouring liquor helps carry the cloth forward into the kier, where mechanical pilers plait it down and distribute it evenly throughout the kier. Heavy weights are used to prevent the cloth being tossed during scouring.

The main object of the scouring process is to remove wax, as the other impurities are more or less readily eliminated in the desizing and washing operations or simultaneously with the wax. About 75% of modern kieriing processes employ a 1-3% caustic soda scour, a method that cannot be used with silk, wool, or certain synthetic fibers. Alkaline salts may be used with this solution in a bath ratio of about 60 gal. of liquor to 100 lb. of cotton, care being taken to maintain adequate caustic soda and sufficient liquid to cover the cloth to prevent air oxidation to oxycellulose. Temperatures of 100-125°C. are regularly used and the kier-boiling operation lasts about 8 hours. Goods that are treated to a lime boil rather than a caustic boil require 2-4% lime (on the weight of the cloth) as  $\text{Ca}(\text{OH})_2$ , with a pressure of 30 p.s.i. Since the lime boil is the first stage in a lime-acid-soda ash sequence, it is slower than the caustic boil.

Kiers are the real bottle neck of the bleaching routine. As few fabrics can be scoured by a single boil, most cloth is turned over and run from one kier to another to give it two boils. Sometimes the goods are then soured by running through sulfuric or hydrochloric acid to obtain better color. The use of rosin soap as a kier assistant has been practiced for over a century. Solvents such as cyclohexanol and decahydronaphthalene mixed with sulfonated oils were marketed as early as 1924, but their value in modern scouring under pressure is debatable. Wetting agents such as the alkyl-naphthalenesulfonates and emulsified pine oil preparations are also used. The most important auxiliaries are, however, the synthetic detergents that have high detergent values, good stability, wetting power, and dispersing action. Examples are the fatty alcohol sulfates and Igepon T. About 8 oz. per 100 gal. is the normal concentration. Difficulties due to calcium and magnesium soaps (cotton wax contains 15-20% free fatty acids) may be dealt with by use of a water-softening plant or by addition of sodium hexametaphosphate or such organic sequestrants as EDTA (ethylenediaminetetraacetic acid, see *Sequestering agents*). Trisodium phosphate and sodium silicate or metasilicate are used to improve detergency in kieriing either with sodium hydroxide or soap.

The need for mild oxidizing agents to prevent vat dyes being reduced to the leuco state when colored woven goods are scoured led to use in the kier of such auxiliaries as *p*-nitrophenol, nitroso-*m*-cresol, and the sodium salt of *m*-nitrobenzenesulfonic acid. Aktivin ( $p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{NCINa}\cdot 3\text{H}_2\text{O}$ ) produces purer whites without deterioration of the cotton. Most goods that are sold in the white state are given two boils, either or both of which may be with sodium hydroxide. Sodium carbonate may be used with colored goods or goods to be dyed, although there is a tendency to use soap and water and a modern wetting agent with colored goods.

Certain types of goods are not kieried but are boiled off with dilute alkali, on either jigs or any of several continuous open-width boil-out machines. The action is usually slower and often not so complete as in the kier. Sodium silicate plus a detergent may be used instead of soap, as the silicate tends to form a soap with the cotton wax. The silicate also possesses wetting powers and increases the stability of the foam produced by the soap. Mixtures of sodium silicate, especially water glass, with soap and solvents are also sold under trade names as kier assistants and are employed to the extent of 0.5% of the weight of the fabric in kieriing or open-width boil-outs.

**Synthetic Fibers and Fabrics.** Scouring and bleaching of synthetic materials are not as important as for the natural fibers. Scouring is simply used to remove the materials which have been taken up in previous processing and is generally accomplished by a mild soap or synthetic detergent treatment. Most rayons are treated in a 0.3–0.5% soap solution containing a little sodium carbonate or trisodium phosphate. Ammonia is often added when cuprammonium rayon is being scoured. Numerous wetting agents and detergents, pine oils, and many terpene preparations are often employed as auxiliaries. With acetate, the alkali and high-temperature sensitivity limits the detergent composition to materials such as neutral soaps and ammonia and temperatures below 85°C. Fabrics containing gelatin size are often desized by overnight soaking in water.

**Wool Carbonizing.** The chemical removal from wool of vegetable matter picked up by sheep during grazing is known as carbonizing. The vegetable matter is destroyed by means of acids, such as sulfuric or hydrochloric, or by salts, such as aluminum chloride, which produce acids by heating to higher temperatures. The vegetable matter is reduced to carbon removed by a mechanical process known as dusting.

Depending on the process used, there are three or four steps. The first operation is steeping or immersion of the scoured wool in a 3–5°Bé. or 4–6% solution of sulfuric acid at room temperature. When the soaking is completed, the excess acid is removed by machine, leaving about 5–6% of actual acid. Then the wool is gradually heated in a dryer or oven to 95°C. until all the water is evaporated and the vegetable matter is charred through loss of chemically combined water. Alternatively, the wool is immersed in a bath of 6–8°Bé. aluminum chloride solution, dried and heated at 120°C. If the aluminum chloride process is used, the neutralizing step that follows baking is unnecessary, but the wool must be thoroughly free of soda before it is treated, as reaction with soda will form a precipitate.

Wool may be carbonized before it is spun or after it is made into piece goods. In either event, any excess acid remaining after the baking and dusting is removed by neutralizing with sodium carbonate after first rinsing the wool in cold water. Great care must be exercised if carbonizing follows dyeing. In general, carbonizing is carried out between scouring and milling and the goods are apt to be wet; if dry, they should be uniformly wet before treatment. Auxiliaries with wetting properties, such as the naphthalenesulfonic acid derivatives and the alkylphenol polyglycol ethers, are frequently used as carbonizing bath assistants.

**Fulling or Milling.** The primitive processes of cleansing fabrics by pounding in the detergent solution are undoubtedly responsible for the discovery that wool will felt, forming a close and compact fiber mass. (See *Felt*.) The milling process is primarily a type of finishing process, but alkaline milling also involves some accompanying cleansing of the goods.

The process is peculiar to the woolen industry because wool alone possesses the peculiar surface scale structure in which the tips of all scales point to the tip of the fiber. Thus the fiber tends to move among other wool fibers in the direction of its root end. The ease of deformation and powers of recovery favor migration by extension in the same way an earthworm crawls. The pressure of the milling machine brings about close contact of the fibers so that the scales find the necessary resistance on each other, the friction causing stretching and the fiber elasticity bringing about contraction and consequent movement. The pressure is intermittent, and the goods naturally show high shrinkage in the process.

Normally 5–10% of soap is used in alkali milling, tallow and palm oil soaps modified with silicate being favored. The fulling stock machine simulates the original trampling process, two stocks or hammers working on the cloth. In the rotary fulling mill pieces run in rope form, passing through two or more heavy rollers into a wooden crimping box. The moisture necessary for the process is supplied in a soap or acid solution, which is applied in a soaping machine just prior to fulling. The soap reduces the friction of the piece in the mill and helps prevent formation of flocks and fulling "streaks." Solutions of pH 4 or lower are used in acid milling, especially where color bleeding may be important. Occasionally "milling in the grease" is employed if disappearance of the shorter fibers is important, for such fibers are bound into the fabric by the process; the soap is formed by action of the fatty acid in the fabric and the alkali applied to it. Oxyethylated tall oil (condensation product with ethylene oxide) is also an acid milling aid.

After fulling, the fabrics are usually scoured by a batch method in dolly washers or in continuous scouring machines. These may have four or five scouring boxes and five or six rinsing boxes. A small amount of synthetic detergent may be added at the beginning of the run, or a small amount of soap and sodium carbonate solution. Usually the goods are thoroughly scoured before milling, but not always, as greasy milling saves a process.

**Silk Degumming.** With silk (*q.v.*) the scouring process is called boil-off, degumming, or stripping and is designed to free fibroin from its impurities, including sericin (silk gum). For certain purposes, however, it is not necessary, or even desirable, to remove all the silk gum. Depending on the relative amounts of gum removed, silk may be classified as: (a) *ecru silk*, from which only 2–5% of the sericin has been removed; (b) *soupled silk*, which contains approximately half of the original gum; (c) *boiled-off silk*, which is free from extraneous matter.

Most finished silk materials are composed of boiled-off silk fibers. Raw silk is degummed in either hank or skein form, although the operation is usually delayed until after the yarns are in the form of piece goods.

The elimination of sericin from raw silk is based on the solubility of sericin in hot alkaline and acidic solutions. Soap, usually made from olive or red oil, is generally used in alkaline degumming, as it has the requisite pH value and imparts a softness and "loftiness" of touch that cannot be duplicated by any competitive detergent-alkali mixture. As silk is acidic in nature, high concentrations of soap are employed in degumming.

Silk is usually degummed by agitating its skeins or fabrics in soap solutions containing 25–50% soap on the weight of the material degummed for 2 hours at 90–98°C. Caustic, soda ash, or sodium sulfite may be periodically added to maintain the solution at pH 10.2, the optimum alkalinity for stripping.

Silk skeins or hanks are often boiled off by soap foam. In this process the skeins are hung in the upper part of a degumming vessel on rotating arms in such a manner that the silk is immersed in foam arising from a boiling soap liquor. By such a procedure little entanglement and damage to silk fibers result.

Synthetic detergents buffered with alkalies, usually combinations of soda ash and tetrasodium pyrophosphate, are frequently used to strip silk fabrics. Such mixtures are rarely used to degum skeins and piece goods but are confined to degumming hosiery and silk specialties. Sulfonated oils and silicates have been used for the same purpose.

Silk unions with wool or acetate rayon are occasionally scoured in hot acid solu-

tion at pH values between 1.6 and 2.0. By such a procedure less damage is produced on the union fiber. Acid degumming is not a common commercial practice.

Ecreu silk is similar to raw silk in feel and appearance. It is generally employed in warps where the friction of weaving is resisted by the harsher fibers. It may also be used as the backing in certain qualities of pile fabrics and in umbrella cloth. Ecreu silk is prepared by agitating silk skeins in soap solutions at 30–35°C. to remove extraneous oils and waxes and bleaching the washed material with peroxide or sulfur dioxide.

Soupled silk is used principally as a filling yarn for fabrics where the filling does not show on the face side. The soupling of silk is designed to remove only those more soluble portions of sericin which act as dye resists. Soupled yarns are produced by washing raw silk skeins for several hours at 35–40°C. in dilute soap or soda ash solutions and bleaching the washed yarns in sulfur dioxide or peroxide solutions.

### Bleaching

**Cotton.** To obtain a pure and permanent white effect, plus level-dyeing properties, cotton goods are generally bleached either with dilute hypochlorite solutions at room temperature, or with peroxide solutions at 80–85°C. The most important of the chlorine bleaching compounds are bleaching powder (see Vol. 3, p. 686), H.T.H. (a purer calcium hypochlorite containing 60% available chlorine as against 36% for bleaching powder), sodium hypochlorite solutions, and Textone (a sodium chlorite product). Hydrogen peroxide (*q.v.*) is usually preferred to sodium peroxide.

The bleaching operation and other "wet processing" operations, such as kier-boiling, mercerizing, dyeing, and some types of finishing, are generally carried on in a separate department or plant known as the bleachery or dyehouse. Often the bleachery prepares its own sodium hypochlorite solutions by passing chlorine into an alkaline solution (caustic or soda ash or a mixture of both).

After the scouring or kier-boiling operation, the goods may be rinsed and given a gray sour, a treatment with dilute acid, commonly hydrochloric, to neutralize any alkali that may remain in the fabric. This is not the same as a white sour, which almost always follows the bleaching operation. Regardless of whether the goods are given a gray sour after scouring, they must be thoroughly rinsed so as to be approximately neutral. They are then squeezed to eliminate excess water that would dilute the bleach liquor or "chemic."

The cloth is bleached by saturating it with a dilute hypochlorite solution, using either a machine chemicking method or the circulation method. The saturated cloth is piled in boxes or concrete bins and kept for several hours. Temperatures are maintained between 55 and 80°F., the available chlorine between 0.1 and 0.6% or between 0.5 and 2.0°Twad., and the pH above 9. From the white bins the cloth is run through a rope washer, then a sour, and finally another wash to eliminate all traces of bleaching powder. The whole process after the kier boil is frequently made continuous by use of J boxes, vertical wooden tunnels built in the form of a printed letter J, which take the place of the bins.

The use of peroxides and other peroxy compounds (see *Peroxides and peroxy compounds*), and particularly hydrogen peroxide, for bleaching not only cotton but also many other fibers, various laces and delicate fabrics, is due in part to its more gentle action.<sup>1</sup> Best results are usually obtained by bleaching in a kier after kier-boiling and washing, some plants even bleaching in the same kier in which the piece



goods were boiled out. Peroxide boiling is done without pressure at 80–85°C., using 0.5–1.5% of 100 volume hydrogen peroxide and an equal amount of sodium silicate to bring it up to a pH of about 10.6. Knitted fabrics and hosiery may be bleached in winch machines. Wetting agents of various types are beneficial in the process, even when it is necessary to bleach in open-width rather than in the kier. Both inorganic and organic sequestering agents, such as polyphosphates and EDTA, are also used as bleach assistants to avoid iron staining and to prevent deposits of insoluble soap films. After bleaching, the goods are washed with warm water and then run through a rope washer. No sour is necessary.

The white sour after bleaching with calcium hypochlorite solutions is needed to eliminate the possibility of calcium carbonate deposition on the fabric. The rope of cloth, after chemicking, is circulated through a dilute hydrochloric acid solution and then thoroughly rinsed with water to remove the sour. Some bleachers take the precaution of "sweetening-off" with dilute sodium carbonate or ammonium carbonate. Antichlors such as sodium bisulfite are also used to remove any traces of hypochlorous acid, lest it tender the goods or diminish the textile strength.

**Linen.** Linen, a strong, lustrous yarn or fabric of smooth-surfaced flax fibers, contains a much higher proportion of noncellulosic matter than cotton does. It is also more susceptible to acids, alkalies, and oxidizing agents. The finest linens and damasks are woven from yarn that has been kiered at low pressure in soda ash solution until about 20% of its weight in the form of impurities is lost. The commoner types of linen cloth are woven from "green" yarn. Both are bleached after weaving.

Linen bleaching is basically similar to cotton bleaching, but the process is much longer and more tedious because of the greater chemical susceptibility of linen. Dilute hypochlorite solutions at room temperature and peroxide bleach at 70–80°C. are both used. The bleaching process for piece goods is more severe than for yarn, but much less stringent than for cotton materials. Indeed, the purifying process may involve ten to twenty operations, including scouring, washing, rinsing, and the various chemicking and souring steps. The demand for milder treatment means a greater number of treatments, not a greater variety. In addition to various alkalies, hypochlorites, peroxides, and hydrochloric acid, chemical kierung and bleaching assistants like those used with cotton are often found of value.

**Rayons.** Although rayon textiles are purified in the same general manner as other cellulosic textile fabrics, there are some minor variations due in part to their being weaker than the native cellulosic fibers. The same bleaching methods and chemicals used for cotton serve rayon, but for shorter times and at lower concentrations, since rayons are even weaker in the wet state. The virtual absence of natural impurities, and the fact that rayon producers supply the yarn in the bleached state, generally mean that only woven and knitted goods, or blends containing natural fibers, require bleaching.

Both viscose and cuprammonium rayons may be bleached with very dilute alkaline hypochlorite solutions. Viscose may also be bleached with hydrogen peroxide. The sensitivity of acetate to high temperatures and alkaline attack has made it desirable to employ hypochlorite solutions, Textone, or sodium chlorite at pH 4.5–5.5, or hydrogen peroxide at pH 8.5–9.5 at 70–80°C. Sodium peroxide, sodium perborate, potassium permanganate, and bleaching powder are also used to bleach rayons or rayon-cotton mixtures.

Bleaching assistants such as the sulfated alcohols, sulfonated castor oil, and vari-

ous other synthetic detergents and wetting agents are usually employed. Soluble oils which are resistant to chlorine are often considered desirable assistants, as they seem to protect the rayon while shortening the bleaching time. Sodium thiosulfate or sodium bisulfite serves as an effective antichlor for goods bleached with hypochlorites. Oxalic acid or bisulfite may be used to neutralize the oxidizing agents when bleaching is completed.

**Silk and Wool.** The chief bleaching agents for silk and wool are sulfur dioxide and hydrogen peroxide. Compounds liberating chlorine, such as the hypochlorites, are not used, for they produce a harsh feel and a yellow color which is accentuated on subsequent washing. Bleaching plays only a small part in wool purification, since most woolen or worsted fabrics need not be pure white. With silk, the amount of gum retained is the normal governing factor because the color is usually in the gum rather than in the silk itself.

Bleaching with sulfur dioxide, or stoving, has been practiced for over two thousand years. The scoured hanks or pieces, if dry, are wetted in a weak soap bath, extracted with water, and suspended over a frame beneath which sulfur is burned to generate sulfur dioxide. It may take 6-8 hours or overnight and is followed by thorough rinsing in water, the last rinse often containing small amounts of Acid Violet or indigo extract. The bleach is not permanent and the odor lingers with the goods, as the chemical is retained tenaciously and may even affect the dyed fabric in storage. Its cheapness and simplicity keep the process in use. Bleaching with solutions of sulfurous acid or acidified sodium bisulfite in a wet steeping process is sometimes done with wool but not with silk, and the effect is no more permanent. Sodium hydrosulfite,  $\text{Na}_2\text{S}_2\text{O}_4$ , a more powerful reducing agent than sulfur dioxide, gives better results with silk than with wool.

Hydrogen peroxide gives a permanent and generally satisfactory bleaching effect on wool and silk, as well as on cotton, rayon, linen, Vicara, and most fibers (except nylon and other polyamide fibers). Most silk and wool and animal hair fibers are bleached by a steeping process in a weak alkaline bath using hydrogen peroxide, or by means of sodium peroxide and sulfuric acid, which produce hydrogen peroxide in the bath. Wool may be treated at room temperatures and up to  $50^\circ\text{C}$ ., whereas silk is usually treated at  $70^\circ$ - $85^\circ\text{C}$ . Ammonia is sometimes used to adjust the alkalinity of the silk bleach to pH 9.6-10, although sodium silicate is generally employed as a stabilizer. With wool, sodium silicate is preferred to ammonia, the pH being kept between 8 and 9, depending on temperature and bleaching speed desired. There are many variations in the processes.

Bleaching is always followed by water rinses. The wet material may then be stoved if a particularly good white is required. Silk may be weighted before or after bleaching; if it is weighted after bleaching, it is important that the fabric be properly acidified before weighting. For this reason ammonia is preferred to sodium silicate in maintaining bleach bath alkalinity with silk. In general, bleaching of silk and wool represents a compromise between loss of tensile strength and improved whiteness, for good bleaching inevitably weakens the yarn.

**Synthetic Fibers.** Nylon and most synthetic fibers normally require no bleaching, as this is done by the producer. In mixed fabrics a permanganate-sulfite bleach is often satisfactory. Hypochlorites are not recommended. Indeed, neither chlorine nor peroxide bleaches can be safely used on nylon or other polyamide fibers because of chemical reaction. Hence it is preferable to employ bleached yarns when nylon unions

are to be manufactured. Recalcitrant stains can be removed by heating with Textractone and acetic acid, however, if done carefully.

### Miscellaneous Treatments

**Mercerization of Cotton.** Treating cotton fabric or yarn with strong caustic soda solutions under tension at low temperature makes the cotton stronger, more lustrous, more absorbent, and more susceptible to dyes. The process is named for its originator, John Mercer, an English calico printer. The material must be held under tension until the bulk of the caustic is removed, in order to maintain its original dimensions and gain the desired luster. Linen, rayon, and bast fibers can also be subjected to a modified mercerizing treatment.

The mercerizing may be carried out at any of several stages in processing, and in either yarn or piece goods form. Yarn is mercerized before bleaching, but piece goods may be mercerized in the gray before or after kiering, or even in the kiered and bleached state. Some processors allow the yarn or fabric to shrink in the alkali to insure thorough penetration, and then apply the tension later, either before or during the removal of the caustic soda. A few mills use a so-called "chainless" mercerizing machine in which the goods are held to width by a series of expanders and revolving cylinders so that no shrinkage is allowed. If no tension is applied to the cotton yarn or cloth during the treatment with strong caustic solution, the cotton will shrink considerably and, upon washing, will show both greatly increased strength and dye affinity, but no luster.

The skein process and the warp process handle cotton in the form of yarn, while the piece goods process, as the name implies, handles fabrics. The most widely used machine consists of a caustic padder in series with a tenter frame, the latter being followed by a washer. The goods pass continuously through the caustic saturator, and the excess caustic is removed by a mangle or squeeze rolls. The function of the tenter frame (stentor or stretching frame) is to pull the cloth out to approximately its original width and then wash out the alkali. The washer after the tenter frame generally consists of several boxes containing lukewarm water (cold water for wool-cotton unions) and dilute acid. If sulfuric acid is used, a final neutralization with ammonia is desirable, but no ammonia is needed if acetic acid is employed.

Caustic soda solutions ranging in strength from 40° to 60°Twad. (19-28%) may be used for mercerizing. For most work, solutions of 50°-52°Twad. are preferred. The period of treatment is usually 30-50 seconds, and the temperature between 0 and 35°C. Kiered yarn does not require the presence of a mercerizing assistant in the caustic, but it often helps. Since caustic solutions, in the concentrations used for mercerizing, have no penetrating power for cotton, unless the cotton has been prepared by removal of the waxes and pectins, the caustic cannot react with the cotton. Most ordinary wetting agents cannot be used as mercerizing assistants to promote wetting and speed of reaction, as they are not sufficiently soluble and stable in moderately concentrated sodium hydroxide solution. Phenolic compounds such as "British cresylic acid" (a special grade of cresylic acid which can be imported from England duty-free) form the basis of most of the successful auxiliaries. Added solvents or coupling agents like cyclohexanol or trichloroethyl ether ( $\text{CH}_2\text{ClCHClOCH}_2\text{CH}_2\text{Cl}$ ) increase the wetting power. Sulfonated ether acids of high molecular weight and dimethyl (hydroxyethyl) laurylammonium chloride are examples of wetting agents that may be used alone. Other surfactants are mixed with the phenolic wetting agent in various proprietary mercerizing assistants.

**Creping.** Lightweight fabrics of silk, rayon, cotton, wool, or a combination of fibers that are characterized by a crinkling or pebbly surface are called crepes. When yarn is given even a moderately high twist, as in the spinning operation prior to weaving, it contracts in length and naturally tends to untwist when free. Because various fibers show differences in swelling properties when wet with water, the tendency to untwist is accentuated when those fibers which swell considerably are wet. This mechanical action is the basis of creping. The great swelling of regenerated cellulose in water has been a major factor in its use for crepes in preference to the more expensive silk.

Creping takes place before bleaching or dyeing. The construction of the woven fabric and its intended end use determine the first wet operation in its processing, for it is obvious that wetting with consequent swelling will have interesting results on the surface structure of the fabric. For most fabrics the yarns are specially prepared by soaking in a solution of a fixative, such as gelatin, and a lubricant, such as emulsified vegetable oil, followed by drying and twisting. The twist of the yarn is then set by steaming, and the yarns are conditioned at, for example, 65% relative humidity before weaving. After weaving, the resultant fabric may be embossed to form by a molding action the pattern or channels in which the fabric will settle. Then the fabric can be wet and creped.

The thermoplastic nature of acetate permits effective embossing, and its relatively low swelling tendency makes possible some very interesting effects on creping, particularly in blends with viscose and other yarns that swell greatly when wet. Embossing is less effective on viscose, but most crepes are embossed as a precautionary measure to correct possible uneven tensions, uneven sizing, and uneven constructions.

A full crepe appearance demands saturation with water rather than simple wetting. The cloth should be wet out evenly, in open-width, without tension, to avoid creases or coarse and uneven shrinkages which would occur in kiering or normal rope scouring. There are several manipulative processes, most of them developments of the original methods used on natural silk. The creping bath precedes scouring, although the two processes may be part of a continuous operation; it may be a hot liquor containing neutral wetting agents, or an alkaline liquor containing soap or caustic soda or both for the purpose of achieving maximum shrinkage and creping, and to increase the affinity of dyes. Thus a liquor might contain 1% of a good oil soap, 0.25% of soda ash, and 0.1% of a fatty alcohol sulfate or fatty acid amide sulfate or other good wetting agent. Some mills may eliminate the soap and soda ash and increase the synthetic detergent, while employing perhaps 0.1% of tetrasodium pyrophosphate as a water softener; the composition used in the setting tanks varies from mill to mill. For maximum creping effects, an alkaline liquor consisting of 20–30 lb. of caustic soda flakes per 100 gal. of water at a bath temperature of 100°F. is usually employed, the concentration of caustic soda being increased for rayon and cotton mixtures.

Textiles that contain starch sizing may be treated first with desizing agents, the subsequent scouring bath completing removal of the size. With acetate warps, and gelatin-sized filling yarns, the bath may employ soap and ammonia with a little solvent. Sodium perborate and soap may be used on oil-sized wefts such as woollen or worsted types. Wetting agents that withstand caustic may be added to alkaline baths to insure adequate penetration. Textiles that have a twist in the filling thread and can be rope-scoured are first set in the open-width; among these are the so-called "multi-filament" crepes, rayon and Beinberg sheers, garbardines, fujis, luanas, ribs and checks,

Shantungs, French crepes, alpacas, and crepe Romaine. Satins, ninons, bengalines, taffetas, and twills are scoured on the jig to prevent breaks and creases which might occur in rope scouring. With wool crepes, strongly acid solutions (for example, 1% sulfuric acid) and temperatures up to 80°C. may be used, as the set at any one temperature is permanent only to water at lower temperature than that at which it was imposed.

Various methods are used for creping, as just noted, for the results can be striking and desirable, or even undesirable. Constructions such as mixtures of highly twisted and slightly twisted yarns, one or both of which may be swelled considerably or only slightly by water, make possible an almost infinite number of effects. Other swelling agents may also be used, as, for example, sulfuric acid or zinc chloride on cotton, phenol hydrate ( $C_6H_5OH \cdot \frac{1}{2}H_2O$ ) or thiocyanates on wool. Solutions which repress swelling, such as 5% common salt or 10% glycerol, may sometimes be added to the creping bath to control the creping. The amount of twist and the hardness of the size on the cloth also have an influence.

**Heat-Setting of Nylon.** The unique "heat-setting" of nylon is accomplished by treating it with boiling water, steam under pressure, or dry heat at temperatures between 98 and 170°C. Setting at 175–190°C. must be employed cautiously and with a much shorter setting time. Nylon fabrics which have not been heat-set tend to acquire permanent wrinkles or distortion during storage or during scouring, dyeing, and finishing, but, if this happens, the fabrics can be stabilized and smoothed out again by setting at a temperature at least 22°C. above the highest temperature to which they were subjected in processing and finishing. Indeed, after nylon lace has been knit on a Jacquard loom, the lace is "set" by this use of a higher setting temperature.

Nylon hosiery is customarily preboarded in the gray on special machines using dry heat or steam at 15–30 lb. pressure for 2 or 3 minutes. Lace webs and warp-knit fabrics are sometimes set by rolling up smoothly while in boiling water, or in steam-pressure chambers. Hot calendering may precede the boil-off of fabrics, so that all the wrinkles may be removed before scouring and boil-setting. Since dimensional stabilization is no problem for fabrics that have been properly heat-set, garments of nylon may be washed and dried without change in dimension or wrinkle. Polyester fibers can also be heat-set and treated like nylon in most other processes.

**Antistatic Finishes.** The effects of static electricity are important to both the processor and the user of synthetic fibers such as acetate, Saran, nylon, acrylics, and polyesters, and indeed to the processor of most other fibers. Thus far there is no general agreement on what constitutes a satisfactory antistatic finish, although most softeners and humectants have antistatic effects. In the plant the effect of these powerful electrostatic surface charges is usually counteracted by maintaining an atmosphere of high humidity or by ionization of the air in the immediate vicinity of the fabric, while rolling or unrolling. A chemical solution to the problem is to apply an antistatic finish.

Antistatic agents may be applied as spin finishes to synthetic fibers immediately after extrusion, may be incorporated in a coning oil, or may be applied at other stages of processing by immersion or spraying. The problems of static disturbance can occur during warping, slashing, winding, spinning, carding, gill reducing, drawing, twisting, weaving, knitting, tentering, cloth examination, tailoring or sewing, and various conditions of final usage by the ultimate consumer. Fortunately, the natural fibers and

rayon are hydrophilic and absorb moisture fairly readily, thus permitting charges to bleed off along the surface to the ground. The protein fibers, also, are hydrophilic. Most of the synthetics, however, have such low vapor absorbeney that static is a constant mill problem, while garments made from them become uncomfortable to wear because of their tendency to cling to the body or clothing and to crackle on moving.

The use of long-chain surface-active agents that impart strong antistatic properties to acetate, nylon, or acrylic fibers is a recent development. Among those found satisfactory are cationic surfactants like the higher alkylamines, long-chain quaternary ammonium halides, alkyl imidazoline hydroacetates, fatty acid carbamides, alkyl betaines, and fatty acid-diamine condensates, as well as hydrocarbon sulfonates, derivatives of polyethylene glycol, and a sorbitan monolaurate polyoxyalkylene derivative. Discretion must be used in applying finishes based on these various products, since certain types may be corrosive, may dust when dry, or have a bad effect on the handle of yarn and fabric. Other types, designed for one operation, may be detrimental in others by modifying the lubricity of the material to cause high backwinding tensions. Those used in processing operations must be capable of being removed whenever their presence may interfere with other operations, as, for example, dyeing. Permanence of a final antistatic finish is normally desirable, but the industry is still debating about products as well as performance requirements since so many variables are involved.

### POSTDYEING OPERATIONS

One of the more recent innovations in the art of textile processing is chemical finishing. The term finishing as applied to textiles was originally used to embrace all chemical and mechanical operations to which yarns and woven and knit goods were subjected to make them marketable. Such a definition would include all textile scouring, bleaching, and dyeing processes, the mechanical operations of calendering, napping, and embossing, and all wet operations employed to apply chemicals to yarns and fabrics. The term, however, has come to have a much more restricted significance, and today it applies only to mechanical processes designed to press out wrinkles and irregularities from fabrics and to imprint special designs and effects, and to operations in which chemicals other than dyes are applied to textiles to produce some particular fabric property. Almost all textiles are now subjected to some form of finishing operation, which may be either mechanical or chemical or, more usually, both.

Mechanical finishing almost always constitutes the final stage of fabric production. The equipment is usually some type of hot or cold calender which simultaneously stabilizes the structure of a textile and produces a new feel and look, especially if a film-forming finish such as starch or glue is present on the fabric. Frequently special forms of mechanical finishing are used to produce some desired appearance on cloth. These operations include: (1) calendering, which produces a flat, shiny, smooth surface; (2) napping, which raises the fibers of a fabric to the surface; (3) embossing, which impresses a raised design; and (4) moiréing, which imprints a water design or water marks. Stretch, pressure, temperature, and steam are the factors involved in mechanical finishing. Chemical finishing agents, such as starches, glues, and oils, are usually required on fabrics to facilitate the mechanical operations and to render their effects more durable.

The chemical finishing of textiles is sometimes assumed to date from World War I, but this date is far too recent. Starches, gums, and other film-forming materials were applied to woven fabrics to facilitate mechanical finishing and make its effects more permanent from the time the weaving and dyeing of textiles evolved from a home craft into an industry. Mercerizing and tin weighting, two of the most important finishing operations, were perfected in the middle of the last century. Little progress was made in the chemical finishing of textiles until early in this century, when manufacturers of modified starches and film-forming substances discovered that such products could be applied to textiles to produce fabrics of improved quality.

Before World War I, textiles could be subdivided into two general classes of materials: those fabricated for ornamental purposes and to appeal to the esthetic senses of the consumer, and those produced for utilitarian purposes. The differentiation between the two classes was due to the fibers used. The luxury fabrics owed their appeal to the beauty and softness of silk filaments. The utilitarian textiles were derived from wool or cotton; wool for materials in which warmth was of paramount importance, cotton for general utility.

Since about 1920, there has been a tendency toward the construction of lighter, less costly materials in which the handle and appearance of quality fabrics are simulated by chemical finishes and other artifices. Some of these creations gave much better service than might have been expected, and established the merits of chemical finishing agents.

At about this time fabrics derived from synthetic fibers were beginning to meet popular acceptance. The early rayon creations possessed many defects and often gave poor service in use, but it was found that many of the inherent weaknesses of rayon could be circumvented by the use of chemicals.

Until about 1900, textiles were used almost exclusively for the manufacture of wearing apparel and the production of household furnishings, coverings, and sundries. The existing requirements of the textile were adequately met by the physical and chemical properties of its fibers. The use of textiles in industry, and for purposes for which they had previously been considered inadequate, has been greatly extended since World War I. This has been made possible by the creation of new synthetic fibers and the discovery that by appropriate chemical treatments and the use of corrective finishes the properties of textiles may be altered to meet industrial requirements. Cotton and rayon fabrics, for example, may be used as umbrella cloth to shed water, in lingerie which absorbs moisture, in draperies and upholstery which inhibit the propagation of flame, in the preparation of fuses which burn, and in the fabrication of wrinkle- and crush-resistant fabrics. The diverse and antithetical properties that may be produced on the same textile fabric are made possible by corrective and modifying finishes.

Chemical finishes are applied to textiles for one or more of the following functions:

- (1) To facilitate mechanical finishing and render its effects more durable.
- (2) To enhance the lure and charm of a fabric. This is accomplished by improving the handle and appearance of a material and by masking the wrinkles and distortions produced during dyeing and covering the imperfections of weaving.
- (3) To increase the utility of a textile. Chemicals which increase the resistance of a cloth to abrasion, chafing, and scuffing and improve the fastness of dyes represent finishes of this class.
- (4) To change the chemical and physical characteristic of a fabric. Finishes which impart water repellency, fire retardancy, and new properties to fabrics belong to this subdivision.
- (5) As sales adjuncts. Many finishes of this class are transient, give no real benefit to the ultimate consumer, and are generally used to impart to inferior merchandise the handle and appearance of more costly materials.

### Fiber Structure

Textile fibers vary chemically, but they probably possess a certain similarity of structural pattern (see *Fibers*). Although no general agreement exists as to the

exact nature of the pattern, it is probable that the basic structure of a fiber consists of long parallel molecular chains oriented along its longitudinal axis and held together by crosslinkages and other physicochemical forces. Exceptions to this basic structure exist. The molecular bundles or micelles in cotton and bast fibers have a spiral rather than longitudinal orientation. Regardless of the micellar arrangement, the external boundaries of the micelles of rayon, acetate, and most natural fibers are porous and permit the entrance of molecules and small colloids, but this layer is impervious to penetration in most of the fully synthetic fibers. This is the basis for the differentiation of fibers into two classes, the hydrophilic fibers (the natural and semisynthetic fibers) and hydrophobic fibers (most of the fully synthetic fibers).

Most of the finishes used in ordinary textile processing are of the external type. They do not enter into the interior structure of the fiber but orient themselves upon the peripheries of yarns and fabrics, either as film-forming sizes or in other forms. They are generally used to add body and weight to a textile material and in other ways modify its handle and physical appearance. Most of the starches, glues, pigments, thermoplastic resins, and oils are the components of external finishes. Such chemicals become tightly affixed to hydrophilic fibers and are not easily removed by physical agencies. The attachment of external finishes to hydrophobic fibers, in contrast, is weak, and comparatively few sizes have the requisite adhesiveness to render them serviceable for finishing hydrophobic fibers.

The intrafiber finishes, which are applicable only to hydrophilic fibers and fabrics composed of them, are used chiefly as correctives to mask or circumvent some inherent textile weakness. In contrast to the external finishes, the internal finishes do not greatly modify the handle or physical appearance of a fabric. The quantity of chemical that may become affixed within the peripheries of silk and rayon filaments is amazing. Silk may be weighted as much as 100% of its weight by stannic chloride (100% addition of "tin"), or even more; viscose will hold up to 80% of its weight as "tin," and it is easy to deposit up to 20% urea-formaldehyde resin within the substance of a cellulosic fiber. Finishes which are affixed or entrapped within a fiber's substance are called internal finishes, and the process by which such finishing is achieved is known as internal finishing.

Chemical finishing operations are not confined to operations in which the chemical and physical properties are modified by the presence of chemical additives. In a few processes the actual chemical structure of a fiber is changed. This transformation of a filament into a new compound is a recent innovation in textile processing and promises to assume increased importance. A partial saponification of acetate fiber (see Vol. 11, p. 566) into cellulose to permit the dyeing of acetate fabrics with direct colors is a common procedure in many dyehouses. Cellulosic fabrics are rendered flame-retardant by phosphation with phosphoric acid and certain phosphorus derivatives (see Vol. 6, p. 553), and the moisture adsorption properties of knit wear made of nylon are improved by chemical modification, leading to the formation of hydrophilic radicals.

Chemical finishing agents may be classified as follows:

(1) External finishes.

- (a) Film-forming sizes—starches, glues, gums, thermosetting and thermoplastic resins, cellulose esters and ethers.
- (b) Softening agents and waxes—sulfonated oils, sulfated alcohols, soaps, and other cationic, nonionic, and anionic softening agents.



- (c) Surface deposits—pigments, drilling agents, fillers, weighting agents, hygroscopic agents.
- (d) Miscellaneous—dye fixatives, moth inhibitors, fire retarders, etc.
- (2) External-internal and internal finishes.
  - (a) Dimensional control—thermosetting resins, urea- and melamine-formaldehyde condensates, formaldehyde, glyoxal.
  - (b) Weighting agents—metallic salts.
  - (c) Corrective finishes—fire inhibitors, dulling agents, moth inhibitors.
- (3) Chemical modifiers of composition of fabric.
  - (a) Mercerizing (see p. 875).
  - (b) Phosphation.

## External Finishes

### FILM-FORMING FINISHES

Many textile materials are submitted after dyeing to some finishing operation in which a film-forming size envelops the yarns and filaments comprising the textile. The finish is used to accomplish one or more of the objectives given on p. 879.

The film-forming finishes are not commonly used alone in finishing textiles, as they are inclined to produce an unpleasant boardy handle. This handle is mellowed by softening agents and plasticizers, usually some type of sulfonated oil or sulfated alcohol. Pigments and clays are often added to the finish as auxiliary components, particularly when the purpose of the application is to mask weaving imperfections.

A great many starches, gums, and glues have been used as film-forming finishes, but the most common in commercial use today are the starches, unmodified and modified, glues, and certain gums. These are being gradually replaced by the cellulose esters and ethers and thermoplastic resins.

**Starches.** The film-forming finishes most commonly used in textile processing are derived from starch (*q.v.*). Starch is essentially a cotton finish, having been used long before the advent of modern finishing to facilitate mechanical processing and to add body and weight to cotton goods.

Corn and rice starches give somewhat similar handles; both impart hard, firm finishes to cotton goods. Corn starches are commonly used in textile processing, but rice starches are not. Goods sized with rice starch, however, take a higher polish than that secured with any other type of starch size; hence it is used by laundries to stiffen collars and cuffs. Wheat starch has perhaps the best adhesive properties of all the commercially available starches and is capable of affixing a greater amount of clay or pigment to cotton goods. Wheat starch, in addition, imparts a full, mellow handle to textiles. Potato starch supplies a smooth, pliable, crisp finish. Some of the modified and hydrolyzed starches have proved their value in textile processing but are not generally serviceable as starch replacements, as they lack the requisite stiffening qualities and adhesiveness. However, they have weighting characteristics and also aid penetration.

Regardless of the type of starch used for cotton finishing, the finish is always modified with a plasticizing agent and occasionally with salts, clays, pigments, and other auxiliaries. The plasticizing agent most commonly used is tallow, usually sulfated. The tallow modifies the dryness and boardiness of the starch film and imparts to cotton goods a smooth, full, mellow handle. Substitution of a sulfonated oil, usually olive or castor, for the tallow is frequently made where a softer, more pliable handle is desired. Sulfated cetyl and stearyl alcohols have replaced tallow as a plasticizer for certain classes of starch finishing.

Plasticized starch finishes are applied to cotton goods to set the effects of mechanical finishing, to add body and weight to the textile, and to affix clays, pigments, and other auxiliaries. Starch is pre-eminently suited to accomplish these objectives. Its films exhibit an exceptional adhesiveness for cotton fibers and can be applied in high concentrations without dusting off. Starches also bind large amounts of clay and other pigments and auxiliaries to textile fabrics. Starch, unlike many natural glues and gums, is white and resists discoloration by heat and ordinary atmospheric agencies.

The chief objections to the use of starch as a textile finish are the ease with which starch is removed from fabrics during laundering, and the opalescence of its films. The opalescence dulls the brilliance of colors and obscures the woven pattern of fabrics. The permanence of starch films can be increased by adding formaldehyde, glyoxal, or one of the urea- or melamine-formaldehyde resins to the starch finishing bath. Care must be exercised in making such additions to avoid the formation of insoluble gels. The opalescence of the starch film may be either an asset or a liability in textile finishing; and this property has largely restricted starch finishing to cotton goods.

Most textile fabrics, particularly the luxury fabrics, owe their appeal to the brilliance of their colors, the softness of their touch, and the clarity of their structural patterns. Such characteristics are not required in cotton fabrics. Cotton goods are inclined to have a somewhat reedy, irregular appearance. The irregularity is restricted by a starch-tallow finish. A complete masking of the defect is secured by incorporating fillers into the finish. The fillers are usually inorganic pigments: china clay, talc, barium sulfate, and calcium sulfate, although dispersions of polystyrene and polymethacrylate resins are beginning to receive some use. China clay is the most commonly used filler. It is white, possesses good covering power, and gives a better and fuller appearance to cotton goods than finishes derived from starch alone.

Although starch is still pre-eminent for stiffening and binding pigments to cotton goods, particularly whites, starch finishing is not so advantageously used on colored goods or on cotton materials such as nets, lace, and veilings whose construction requires some support without substantial filling. On colored cotton goods the modified starches are often substituted for the starch, at least in part. The modified starches penetrate more deeply into the fiber and produce brighter color effects. It is often desirable to preserve the structure of laces, ribbons, and similar constructions. Gelatin, glues, and the natural film-forming gums are used for this purpose as they produce transparent films. The thermoplastic resins are gradually replacing the natural glues and gums in the finishing of these specialties.

Although maximum softness and pliability are the conventional requirements of textiles derived from the synthetic fibers, certain classes of material are prepared from them that require body, crispness, and a sharpness of touch. Such materials include marquisettes, georgettes, certain types of crepes and veilings, and specialties such as laces and ribbons. Concentrated gum arabic and gelatin or glue solutions were formerly extensively used to produce the desired properties, but here also thermoplastic resins have largely replaced the natural finishes.

Silk materials, particularly the lighter, more flimsy constructions, require additional body and drape and, unlike the newer synthetic fibers, can acquire considerable amounts of size without impairing their silkiness of touch.

**Gelatin and Other Proteins.** Gelatin (*g.v.*) was formerly extensively used in silk finishing and is still an important ingredient in many types of finishing compositions. It is generally used with sulfonated oils, weighting agents, pigments, and

other auxiliaries. The gelatins and glues generally impart a full, round handle to silk fabric. Where a sharper, thinner touch is desired, gum arabic is often used as a glue replacement. Casein, soybean protein, and albumin have been occasionally used instead of gelatin. Most of the protein finishes are high in cost and tend to yellow and discolor fabrics during aging.

**Gums.** Gums (see *Gums and mucilages*) occupy a very minor position in finishing today. They were formerly much more extensively employed in textile processing. The chief gums in use are gum arabic, gum tragacanth and locust bean gum (Tragacanth).

Gum arabic is used in finishing silk and rayon fabrics. It is probably the most transparent of the natural film formers and gives a papery handle to fabrics without perceptibly reducing the brilliance of the colors or obscuring the fabric structure. Gum tragacanth and locust bean gum have finishing properties somewhat similar to gum arabic. Their solutions are more viscous than those of gum arabic, and they are hence serviceable only for supplying light finishing effects. They tend to impart much more body and plumpness to rayon than gum arabic. Gum tragacanth solutions do not carry and affix pigments to textiles effectively; locust bean gum surpasses tragacanth in this respect. Gum tragacanth is used chiefly in finishing mercerized shirtings. Gums derived from Irish and Iceland moss, karaya, algin, and quince seeds have received limited applications in textile finishes. Such gums cannot ordinarily be applied in concentrated solutions and are used chiefly in the processing of knit goods with other auxiliaries to produce a modicum of additional body to the fabrics.

**Thermoplastic Resins.** Starch and the natural film-forming glues and waxes are being gradually replaced by the thermoplastic synthetic resins. The advantages of the newer synthetics are:

- (1) They possess superior adhesion to fabric surfaces. This is particularly true with the hydrophobic fibers such as nylon and Orlon, which do not adhere well to natural sizes.
- (2) They form transparent films and hence restrict the brilliance of dyes and luster and pattern of fabric to a lesser extent.
- (3) They bind pigments and auxiliaries to textiles.
- (4) They resist discoloration and changes during aging.
- (5) Certain synthetics are durable to laundering and dry cleaning and maintain their finishing virtues throughout the life of a fabric.
- (6) Certain resins protect fabrics against abrasion, scuffing, and other factors incidental to wear, thus extending their lives and period of utility.
- (7) Synthetics can be tailored to meet any ordinary textile requirement of touch.

A large number of synthetic resins are theoretically serviceable for textile-finishing purposes, but those in actual use are confined to: (1) the polyvinyls, chiefly polyvinyl acetate and polyvinyl alcohol; (2) the polystyrenes; (3) the polyacrylates and polymethacrylates. (See *Acrylic resins and plastics*; *Styrene resins and plastics*; *Vinyl compounds, resins, and plastics*.) The thermoplastic resins were first produced as bulk polymers or as solutions in organic solvents, and the fact that they had to be handled from organic solvent systems excluded them from the field of textile processing. Few textile processing plants are equipped to handle volatile solvents, and it was not until aqueous resin dispersions (emulsions) were produced that the thermoplastic resins were seriously considered textile finishing agents.

The preparation of the resin dispersion is still more of an art than a science, but products to meet almost any desired finishing requirement are being prepared. The

dispersions are generally produced by dissolving the water-soluble monomer in water and adding dispersing agents, stabilizing agents, and a catalyst. By heat and other agencies the monomer is converted into dispersed particles of insoluble resin serviceable for textile finishing. The properties of the resin dispersion depend upon the particle size of the resin, its chemical nature, and the electrical charge present on the colloid. These factors are conditioned by the dispersing agent, the pH of the emulsion, the stabilizing agent, the methods of mixing, and other factors. The dispersing agent may be anionic, nonionic, or cationic, and its characteristic electrical charge is imparted to the dispersed resin particles. The size of the colloidal particles in the dispersions varies from 0.4 to 10  $\mu$ .

Although it is difficult to characterize with any degree of exactitude the influence of these factors in textile processing, the following statements can be made at least qualitatively.

(1) Anionic, nonionic, and cationic emulsifying agents usually convert resin colloids into negatively charged, neutral, or positively charged particles, respectively. Although the colloids may be affixed and oriented to fabrics regardless of the sign of their electrical charge, anionic resin colloids are often repelled by textiles in the finishing bath and have a low rate of exhaustion. Conversely, cationic colloids may be adsorbed so avidly that nonuniform distribution of finish is obtained on textiles. This property has tended to exclude cationic resins from conventional finishing practice. Nonionic resin emulsions (those dispersed with nonionic emulsifying agents) occupy an intermediate position and are more generally used in the preparation of industrial textile finishes. Anionic resins on the whole produce softer and more durable finishes than the nonionic.

The particle size of the resin colloids is of much importance in textile finishing. Dispersions of larger particles exhaust more readily onto textiles from the finishing bath and produce a much firmer and more bodied handle than solutions of finer particles do. The latter, however, penetrate more deeply into the structure of yarns and are more resistant to removal by ordinary laundering and dry cleaning.

Although thermoplastic resin dispersions are composed of solid resin particles, the discrete particles merge on drying to form transparent continuous films. These often orient themselves to fabrics in such a way that a durable anchorage results which resists removal during ordinary laundering. The factors involved in this mechanism have been only incompletely investigated. It would appear that most resins are supercooled liquids, which on contact slowly fuse together irreversibly to produce strong clear films. The flow of the resin colloids and their orientation to textiles are accelerated by elevated temperatures and the presence of plasticizing agents or solvents. The flow of certain highly polymerized resins, such as the very hard polymethacrylate, polystyrene, and polyvinyl chloride particles, is so slow that the particles do not merge into films under ordinary finishing processing conditions and, when applied to textiles from aqueous dispersions, dry in the form of discrete particles. Such deposits often act as delustering agents.

*Polyvinyl acetate* dispersions are probably more extensively used in textile finishing than any other thermoplastic resin. The dispersions are used to impart stiffness, body, and weight to fabrics, to protect textiles against the mechanical abrasive agencies resulting in wear, and to bind pigments and other external finishes to the surfaces of fibers. Polyvinyl acetate finishes are outstanding in their freedom from discoloration, their resistance to removal during laundering, the variety of textiles to which they can be effectively bonded, and the versatility of their finishing effects.

Although polyvinyl acetate can be used as a finishing agent for almost any type of fabric, it is used chiefly on rayons, silk, and so-called luxury fabrics fabricated from the hydrophobic fibers. The polyvinyl acetate resins are not commonly used to finish cotton broad goods but are occasionally used in the finishing of cotton laces and veilings, where some additional strength and body are required and it is desired to preserve the structural clarity of the fabric pattern.

Polyvinyl acetate resin dispersions are employed chiefly as a general-utility finish to produce stiffness and a crisper handle in materials such as sheeting and dress goods and particularly in the processing of fabrics such as ninons and marquisesettes when maximum body is required. The nonionic large-particle emulsions are used for general-utility finishing for maximum stiffening effects; the anionic, colloidal emulsions are used where maximum durability to laundering is of major importance. The durability of polyvinyl acetate finishes can be enhanced by the addition of formaldehyde or glyoxal to the finishing solution or by exposing the finished fabric to a temperature of 300°F. for a few minutes. Emulsions containing between 1 and 5% of polyvinyl acetate are commonly used for general-utility purposes. For finishing open-weave fabrics or for hard, dry finishes (marquisesettes, buckrams, ribbons, etc.) resin emulsions of 50-60% resin are frequently employed.

Polyvinyl acetate resin dispersions are extensively employed as auxiliaries in fixing pigments, clays, water repellents, and surface deposits on fabrics and as an adjuvant with starch in cotton processing.

Few thermoplastic resins except the polyvinyl acetates are extensively used in textile processing and most are employed in the production of some novelty or specialty. The *acrylic acid copolymers* and methacrylate homologs have properties similar to those of the polyvinyl acetates and are useful for much the same purposes. The higher cost of the resins has limited their applications in finishing. Both are used in the finishing of nylon hosiery, and the unplasticized methacrylate resins have some use as a dulling agent. The *unmodified polystyrene* dispersions do not form films but dry to a white powder. They are used principally as delustering finishes in conjunction with polyvinyl acetate dispersions. The *plasticized polystyrenes* do form films and are occasionally used as a substitute for polyvinyl acetate. The *polyvinyl chlorides* and the *chloride-acetate copolymers*, although not commonly used in ordinary finishing, are used in shower curtains, certain types of coated fabrics, and fire-retardant coatings. *Vinylidene chloride copolymers* are even more potent flame inhibitors, but it is difficult to stabilize these resins against discoloration during aging. The *butadiene-styrene copolymers* and *acrylonitrile copolymers* form tough, flexible films which show adhesion to fibers and a good resistance to solvents. Aqueous dispersions of these resins have been used in textile back-fillings and plush and upholstery backings. The acrylonitrile copolymers are used to produce a loom finish for denims.

**Thermosetting Resins.** The thermosetting resins are of far greater importance than the thermoplastics in the finishing of textile fabrics. Most of them are either urea-formaldehyde or melamine-formaldehyde condensates and are the most versatile of all chemical finishing agents. The alkyl resins, particularly the polyglycerol phthalates, also have some applications.

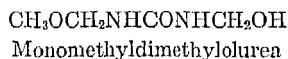
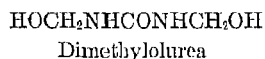
Unlike the thermoplastic resins, which are usually applied to textiles in the form of dispersions of fully polymerized particles, the thermosetting resins are generally applied as water-soluble monomers or intermediates which are polymerized on the fabric by heating with catalysts at 280-320°F. Dispersions of completely polymerized

urea-formaldehyde resins, however, have some application in textile finishing. Thermosetting resins are produced by a stepwise polymerization in which the monomers react with each other and with condensation products to form resin intermediates of increasing complexity. The intermediates, in the absence of catalysts, are stable compounds that can be used industrially as finishing agents. Thus, from the same two precursors a whole gamut of resinous products can be synthesized, almost any of which is important in textile finishing. The monomers and simpler polymers are useful as corrective finishes in inhibiting wrinkle formation and securing dimensional control, the film-forming intermediates for supplying weight and body to textiles, whereas the higher-polymer dispersions act as dulling agents. Even the resin precursors, urea (*q.v.*), melamine, and formaldehyde (*q.v.*), are employed in textile finishing: urea as a weighting and hygroscopic agent, formaldehyde as a fixative for dyes and starch, and as a preservative and crush inhibitor; and melamine as a fume arrester for acetate colors.

The *urea-formaldehyde* and *melamine-formaldehyde resins* (see *Amino resins and plastics*) are essentially finishing agents for cellulosic fibers. They are without color, anchor themselves tenaciously to viscose and cotton fibers, and the monomers and lower polymers are even capable of impregnating the peripheral wall of cellulosic fibers to become for practical purposes an integral part of the textile.

Urea-formaldehyde resins do not form a particularly adhesive attachment to the fibers of acetate rayon and the hydrophobic textiles such as nylon, Dacron, and Orlon, and hence have only a limited use in finishing fabrics derived from such fibers. The melamine-formaldehyde condensates, which bond better to hydrophobic filaments, are more extensively used.

Modified urea-formaldehyde and melamine-formaldehyde resins have recently been synthesized. The modified resins are for the most part alkylated resins in which the hydrogen of the methylol is replaced by an alkyl group, usually methyl.



The modified resins possess an improved affinity for hydrophobic fibers and an ability to inhibit the shrinkage of wool. Urea-formaldehyde and melamine-formaldehyde resins of all types are unstable and are readily polymerized by heat and acid and alkaline catalysts to form hard, insoluble and infusible higher polymers. The urea- and melamine-formaldehyde thermosetting resins are usually subdivided into at least five classes: (1) the precondensates, (2) the low and partially polymerized resins, (3) the so-called acid colloids (the most highly polymerized stable resins), (4) the colloidal dispersions, (5) modified urea- and melamine-formaldehyde condensates. The precondensates and low polymers are usually employed in textile finishing as internal finishes to impart crush and dimensional control properties to cotton and rayon piece goods (see pp. 899,905), whereas the more highly polymerized resins are used as external finishing agents.

Although the urea-formaldehyde resins and their melamine-formaldehyde equivalents are frequently regarded as correctives to circumvent some inherent defect of a textile, they are extensively employed to produce body-building films about fabrics, to affix pigments and certain classes of dyes, to render starch and gelatin finishes wash-resistant, to increase the durability of transient water repellents, and to produce special finishing effects.

Urea- and melamine-formaldehyde resins are of variable structure and may be tailored to meet almost any finishing requirement. The monomers and lower polymeric forms of resin impart a durable bulky handle to rayon and cotton wear which may be modified to a silk-like touch by suitable softening and hygroscopic agents. With higher polymerization the handles imparted to textiles become increasingly stiffer and more crisp. The acid colloids, the highest polymerized resins suitable for finishing purposes, impart a degree of stiffness and wash durability unmatched by any other available resin.

The urea- and melamine-formaldehyde resins are rarely used alone as surface finishes; the handle they impart to textiles is too boardy and crisp to meet with commercial acceptance, and the sized fabrics are inclined to be brittle and tear easily. The defects of touch and strength are obviated by a plasticization of the resinous film with softening and hygroscopic agents and, for special purposes, with clays, talcs, and waxes. The choice of the softening agent has a marked effect on the character of the handle secured. Sulfonated tallows and waxes when applied with the resin produce a firm, waxy touch, whereas the nonionic and cationic softening agents give a much silkier, limper handle. The latter type of plasticizing agent is almost invariably used with the urea- and melamine-formaldehyde resins in finishing materials derived from hydrophobic fibers.

The most salient characteristic of fabrics finished with thermosetting resins is their spring and "life." Such textiles when compressed spring back to their original position when the compression force is removed. This property is highly esteemed in many types of merchandise and accounts for the popularity of urea and melamine resin finishes.

Although the unmodified urea- and melamine-formaldehyde resins are essentially finishes for cellulosic fabrics, they are frequently used to strengthen and size nets, laces, ribbons, and specialties made from acetate rayon, nylon, and other synthetic fibers. The bond between the resin and such fabrics is poor, and the finish is likely to scratch and flake from the textile during use. A more durable bond between hydrophobic fabrics and resin is secured by the use of the modified alkylated resins. The alkylated melamine-formaldehyde condensates are more frequently applied to hydrophobic fibers than the alkylated ureas, as they anchor themselves to the textiles more securely to produce a heavier finishing effect. The flammability of nylon nets and laces is enormously enhanced by heavy alkylated melamine-formaldehyde resins and often constitutes a fire hazard. Modified thiourea-formaldehyde resins are occasionally substituted for the melamine resins in the finishing of hydrophobic fibers where maximum flame resistance is a requirement.

*Alkyd Resins.* The only thermosetting resins other than the urea- and melamine-formaldehyde and their equivalents which are extensively used in textile finishing are the alkyd resins (*q.v.*). The resins of this class may be obtained in diverse polymeric states, the lower polymers producing a soft handle, the more highly polymeric structures a firmer, stiffer handle. Unlike the urea-formaldehyde polymers, the alkyd resins are not correctors of fabric defects but are used in finishing to supply a textile with body and weight. The alkyd resins bond firmly with most types of textile fabrics.

The higher polymers are used chiefly in textile finishing. Fabrics impregnated with such polymers acquire a crisp, papery handle resembling that imparted by gum arabic. The most interesting characteristic of alkyd resin finishes is the transparency of their films on textile fabrics. These finishes are among the few that do not lower the

luster of textiles, or impair the brightness of colors. Alkyd resin sizes are not durable to laundering, but the washfastness of the resin is improved by the presence of heavy metallic salts in the finishing bath. The resin is used chiefly as a ribbon finish. It is used to a limited extent in the finishing of nylon knit goods and in the processing of georgettes.

**Cellulose Derivatives.** Considerable interest has been aroused at various times in the use of cellulose derivatives (*q.v.*) in textile finishing. Although all members of this group of compounds are derivatives of cellulose, the characteristics and properties of the various members are so dissimilar that the group can be subdivided as follows: (1) alkali-soluble cellulose solutions, (2) water- and alkali-soluble cellulosic ethers and esters, (3) dispersible cellulosic ethers.

*Alkali-Soluble Cellulose Solutions.* Although cellulose solutions are prepared from inexpensive raw materials, their use in the wet finishing of textiles has been limited by technological difficulties in the preparation of solutions of uniform composition and by difficulties in applying the solutions to textiles. It is probable that with the evolution of newer types of thermoplastic resins interest in cellulose solutions as textile finishing agents will decrease.

Cellulose is capable of being solubilized by a limited number of solvents. Most of these are strongly alkaline and include such inorganic complexes as cuprammonium hydroxide, alkaline sodium zincates, and certain organic bases such as benzyltrimethylammonium hydroxide. Cellulose can also be rendered soluble by converting it into a xanthate. These solubilized forms of cellulose act as finishing agents. They may be impregnated onto fabrics from a quetsch or pad and affixed by a subsequent acid treatment. Fabrics finished with cellulose solution have a rather thin handle, resist abrasion, are extremely resistant to laundering, and are probably the most durable of all textile finishes. Interesting effects may be secured by combining cellulose finishes with certain mechanical operations; cotton may be linenized and important luster effects can be secured.

*Water- and Alkali-Soluble Ethers and Esters.* Methyl celluloses and particularly hydroxyethyl celluloses are of much greater importance in textile finishing than the cellulose solutions. Although the methyl celluloses exhibit good film-forming properties and are potentially serviceable as finishing agents, they have found little application in finishing. They are used in the preparation of printing pastes and as yarn sizes.

Great interest has been aroused in the use of the hydroxyethyl celluloses in finishing. Three hydroxyethyl celluloses are prepared commercially containing approximately one, two, and eight ether radicals per four glucose residues, respectively. The lowest etherified member is insoluble in water, alkali, and organic solvents and is not used in textile processing. The more highly esterified esters are alkali- and water-soluble, respectively, and each is a valuable finishing agent.

The alkali-soluble hydroxyethyl cellulose ethers are among the best durable finishes. They are applied to cotton goods and rayons, particularly spun rayon, to produce the hard crispness of handle usually associated with linen. Softer effects may be secured by the incorporation of waxes and waxy soaps, often bleached beeswax emulsion, in the finishing bath. Occasionally china clays and other fillers are included in the bath to obscure yarn and weaving imperfections.

The finish imparted to fabrics by alkali-soluble hydroxyethyl cellulose is one of the most durable obtained. It normally survives the life of a fabric and is so permanent



that it may be applied either before or after dyeing. The application of the ether to textiles is much more involved than conventional finishing practice. The hydroxyethyl cellulose (1-5% strength) is generally prepared in alkaline solution containing 5-10% caustic. Fabrics at open width are passed through this solution and subsequently neutralized with acid to set the resin. Wrinkles and creases must be avoided during the neutralizing to avoid the permanent set of an imperfection into the cloth.

Alkali-soluble hydroxyethyl cellulose imparts a stiff linen-like finish to textiles and protects the fabrics against wear and mechanical damage. The finish is generally applied to shirtings, sheetings, and materials on which a linen-like finish is desired. Damask and jacquard weaves are commonly processed with alkali-soluble hydroxyethyl cellulose not only for the linen effects but also for the nonlinting qualities produced.

The water-soluble hydroxyethyl celluloses are used chiefly as thickening agents and in knit goods sizes to impart additional body.

*Dispersible Cellulosic Ethers.* Many cellulosic ether dispersions, particularly those prepared with ethyl cellulose, have been employed in textile finishing to give durable, abrasion-resistant fabrics. Such dispersions have not achieved much commercial success because of a lack of emulsion stability in the presence of traces of electrolytes.

#### SOFTENING AGENTS

With the possible exception of luster, no physical characteristic of textile fabrics is more highly esteemed than softness. Silk owed its preeminence as a fiber to its sheen and softness. Although silk, for economic and other reasons, has been largely replaced by the rayons and synthetic fibers, none of the replacements even approximates the feel of silk. Enhanced softness can be secured on textiles by the use of softening agents. The softening agents likewise plasticize and mellow the handle of film-forming chemicals, such as starch and the thermoplastic resins, increase the life and utility of a fabric, and rejuvenate overworked and overbleached textiles.

The mechanism of textile softening depends on many factors. Although structural factors such as the size, twist, diameter, and character of the component yarns and the weaving design determine the inherent feel of a fabric, an estimate of its handle is based on its thickness, its surface lubricity, flexibility, compressibility, and elastic recovery from a compressive force.

**Action of Surface-Active Agents on Textiles.** Many of the softening agents are surface-active agents (*q.v.*) The hydrophilic-hydrophobic balance of these softening agents is more predominately hydrophobic than in most surface-active compounds. The hydrophilic forces should be potent enough to produce solubility but sufficiently weak to allow orientation of the hydrophobic end of the molecule to a textile fiber.

The hydrophobic groups most generally used in the preparation of softening agents are the pentadecyl ( $C_{15}H_{31}$ ), heptadecyl ( $C_{17}H_{35}$ ), octadecyl ( $C_{18}H_{37}$ ), and heptadecenyl ( $C_{17}H_{33}$ ) radicals or their equivalents, although less complex members of the alkyl series, such as dodecyl ( $C_{12}H_{25}$ ), are used to some extent. Softening agents containing pentadecyl and heptadecyl radicals are inclined to impart bulkier handles and good surface lubricity to textiles. The heptadecenyl and lower alkyl radicals furnish greater limpness and in some cases even an undesirable "ragginess."

Most textiles are anionic (wool under acid conditions and a few hydrophobic fibers excepted) and therefore tend to repel anions and attract cations. As a conse-

quence, there is little exhaustion of an anionic softening agent from a finishing bath. About all the agent acquired is that present in the water of the finish adhering to the fabric after drying. This orients itself to the textile in a characteristic manner; the hydrophobic portion, which tends to envelop any material that it can wet, sheathes the fibers in an oily or waxy film, while the hydrophilic portion of the softener coats the film externally like a microscopic "suede." This "suede" has little effect on the organs of touch and imparts little surface lubricity. As a consequence, anionic softening agents, although they impart enhanced pliability and flexibility, furnish little surface lubricity. This deficiency is partially circumvented by blending fats and oils into the anionic softening agents. Since little anionic softening agent is absorbed by a textile during its passage through a finishing bath, high concentrations are required to produce optimum softening effects.

Cationic softening agents are attracted to negatively charged textiles in aqueous solutions. The hydrophilic portion of the softening agent combines with negatively charged radicals in the intramolecular structures of the filaments, firmly anchoring the hydrophobe, which sheathes the fibers as a film. Thus with cationic softening agents the hydrophobe constitutes the external phase of the oriented structure, the hydrophile the interior. As a consequence, cationic softening agents tend to impart to textiles a soft, well-lubricated, and pliable surface. Since cationic softening agents are attracted to textiles, relatively low concentrations are required in the finishing bath to produce the requisite softening effects.

Being electrically neutral, nonionic softening agents are little affected by the electrical charge present in textile fabrics. Properly designed nonionic chemical structures have excellent softening properties; emulsified raw oils or waxes are often incorporated with a nonionic softening agent to enhance the softening effects of the product.

Softening agents may be divided into the following classes: (1) emulsions of oils, fats, and waxes; (2) soaps; (3) sulfonated oils; (4) sulfated alcohols; (5) fatty acid condensation products; (6) substituted ammonia complexes.

Before the development of the synthetic softening agents, soap-oil emulsions constituted the softening agents used in textile finishing. Two general types were used. Silk fabrics were generally softened with emulsions of olive oil, whereas superfatted tallow soap dispersions were employed in cotton finishing. As such emulsions do not produce optimum softening effects and are inclined to be unstable, they have been largely replaced by more potent agents.

Oil emulsions, however, still receive limited application in textile finishing, but their formulations have changed. The oil phase of the emulsion is generally a saponifiable-mineral-oil blend; the dispersing agent a nonionic surfactant or an anionic emulsifying agent stable under neutral or even acidic conditions. Such agents are usually stabilized against the development of rancidity and discoloration during aging and often contain sequestering agents to permit use of the emulsion in hard water. Although oil emulsions are more commonly used in the preparation of yarn sizes, they are occasionally employed with other finishes to supply surface lubricity to fabrics, particularly to knit goods composed of cotton or rayon.

**Soaps.** Soap (*q.v.*) is extensively used as a finish. Many of the so-called sulfonate tallows used with starch in cotton finishing are essentially superfatted stearic acid soaps. Soap, usually derived from a purified olive oil, is still used in finishing certain quality silks and particularly fabrics dyed with vat colors. Soap imparts to silk material a bulk and "loftiness" difficult to obtain with synthetic softening agents.

Soap-tartaric acid or soap-sulfuric acid mixtures are rather commonly used in silk finishing to produce seroop (see p. 893).

There has been a revival of interest in the use of soaps as softening agents since the discovery that complex stearic acid-glyceride soap synthetics (Profine, a mixture of glycerol monostearate and stearic acid soap) impart a smooth bulky handle to bleached cottons and rayons without dulling the clarity of the bleach or changing the brilliance of optical bleaches. These soaps are extensively used in softening bleached cotton and rayon knit goods.

**Sulfonated Oils.** The use of sulfonated oils in finishing has declined recently. They are usually derived from olein-base oils such as teaseed, olive, and sperm, from castor oil, and from tallow. The oils are usually sulfonated to secure a preponderance of hydrophobic characteristics (only enough sulfation to produce easy solubility). More highly sulfonated oils usually possess inferior softening properties. A sulfonated oil is not a single compound but is a mixture of sulfonated oil, sulfated oil, raw oil, lactones, glycerol, and oil decomposition products. These in solution yield chemically complex micelles which function as hydrophobic colloids.

Sulfonated oils differ from most soaps and most synthetic softening agents. Most surface-active agents have a long hydrophobic tail attached to a polar head, but with the sulfonated oils the polar group is in the center of the molecule. It is claimed that such a molecular architecture, other things being equal, permits a greater accumulation of fatty matter on a fabric surface. Oleic acid derivatives are unsaturated compounds and as such tend to oxidize and change during aging, becoming yellow and rancid. These characteristics are inhibited by the addition of antioxidants, preservatives, perfumes, and other ingredients. Such correctives are used in most of the sulfonated oils of commerce.

Most sulfonated oils tend to give textiles a soft, raggy handle. They increase the flexibility of fabrics but are of only minor importance in imparting surface lubricity. This deficiency is corrected by the addition of mineral oils, raw and half-sulfated fatty alcohols, or other adjuvants. Sulfonated oils are excellent plasticizers for starches, glues, gums, and other film-forming sizes. The sulfonated tallows produce a fuller, drier, waxier handle than the oils and are employed where such an effect is desired. They are extensively used with starch in cotton finishing. Neither the sulfonated oils nor the tallows are widely used in the finishing of woolsens or fabrics made of hydrophobic fibers.

**Sulfated Fatty Alcohols.** Partially sulfated fatty alcohols (alcohols such as cetyl or stearyl, derived by reduction of fatty acids) are valuable softening auxiliaries in finishing operations. Unlike the sulfonated oils, most of their virtue is their surface lubricating action. They may be used as textile softeners either alone or with waxes, oils, and other agents to produce some special effect. They tend to produce a smooth, waxy handle and are effective softeners even when applied to textiles in low concentrations.

Several interesting "synthetic sulfonated and sulfated oils" have been prepared from secondary alcohols which are claimed to produce the virtues of both the alcohol and the oil. As in the sulfonated oils, the hydrophilic radical is in the middle of the molecule, and it is claimed that extremely low concentrations of softening agent are required to produce optimum effects.

**Fatty Acid Condensation Products.** Although soaps, sulfonated oils, and the sulfated fatty alcohols, often fortified with raw and mineral oils and other auxiliaries,

constitute most of the anionic softening agents used in textile finishing, sulfated and sulfonated fatty amides and amines, ethers and esters have limited application. The effectiveness of such compounds depends on the type of fatty radical present and its hydrophilic-hydrophobic balance. For the most part these condensates offer few advantages over the softeners previously described.

**Nonionic Softening Agents.** The nonionic softening agents, produced by the condensation of fatty acids or fatty alcohols with ethylene oxide, are among the most useful finishing auxiliaries. The length of the polyethylene oxide chain in the molecule can be modified to secure any hydrophilic-hydrophobic balance and produce surface-active agents approximating the anionic softening agents in effectiveness. The stability of the nonionics, rather than their softening action, makes these compounds important.

The polyethylene condensates are soluble in either acid or alkaline solutions, in hard water, in solutions of heavy metallic salts and pigments, and even in the presence of anionic and cationic materials. Unlike the anionic and cationic softening agents, which have stability limitations, the nonionics are stable and exert their softening effects in the presence of almost any finishing agent used in textile processing.

The nonionic softening agents are used alone chiefly in finishing compositions, for which anionics and cationics are poorly adapted (for example, weighters and pigments). The nonionics also are used with anionic and cationic softening agents to improve their stabilities and produce some special softening effect on textiles.

**Cationic Softening Agents.** The cationic softening agents are the only type of compounds which favorably affect all the properties that contribute to the softness of a textile: its flexibility, compressibility and elastic recovery, and surface lubricity. However, they possess many inherent finishing defects: they react with anionic gums and finishes to form sticky, insoluble conglomerates, have no plasticizing action on many film-forming finishes, and tend to discolor and yellow whites, particularly bleached whites. The effect of many cationics on dyes may be even more serious; the color shade is often turned and there is frequently a loss of colorfastness. However, the softening effects that cationics impart to rayons and the hydrophobic fibers are so superior that their use in the finishing of broad goods is extremely important.

The inherent defects of the cationic softening agents may be partially avoided by altering their chemical structure. Condensations of cationics with urea, triethyl phosphate, and other reagents make them less cationic without destroying their substantivity for anionic fibers or reducing their softening characteristics. These modified softening agents are known as substantive softening agents. They are of particular interest in minimizing the harshness caused by synthetic resins.

The cationic water repellents, stearoxymethylpyridinium chloride and stearamido-methylpyridinium chloride and their equivalents, are also effective durable softening agents (see *Waterproofing*).

**Water and Hygroscopic Agents.** Water is an excellent softening agent for many classes of textiles. This accounts for the fact that fabrics are generally softer and more pliable in the humid days of summer. This is particularly true of wool. Steaming of wool is intended to impart greater softness to woolsens and increase their water content. Cotton goods and rayons are also frequently steamed. Such devices for increasing the softness of fabrics are extremely transient and too fugitive to benefit the ultimate consumer. The durability of the effect may be increased by the use of hygroscopic agents. Glycerol, ethylene and diethylene glycols, urea, glucose, and salts such

as potassium acetate, zinc chloride, magnesium chloride, and sodium sulfate are often added to textiles to increase their moisture retentivity, to supply weight, and to reduce static.

The processes and chemicals designed to enhance the softness of textiles by increasing their moisture content have some hazards. Excessive moisture stimulates the growth of molds and mildew on fabrics, and the alternate acquisition and evaporation of moisture through changes in the weather result in shrinkage and distortions in the shape of apparel. Although the growth of microorganisms may be arrested by the use of antiseptics, no means of restricting water evaporation from cloth in dry weather has been found. The addition of limited amounts of hygroscopic agents to fabrics is, however, a valuable plasticizing and softening aid to many types of finish.

#### SPECIAL OIL AND WAX FINISHES

**Seroop.** Oils and fats and their derivatives are regarded as textile softening agents and lubricants. Yet under certain conditions of application some oils have a reverse effect, inducing intrafabric friction and producing during compression a crunchy feel and a rustling sound known as seroop. Seroop was at one time considered an exclusive property of silk and was produced by soaking silk fabrics in a soap solution, acidifying the soaped material in a tartaric or weak sulfuric acid solution, and drying the textile without rinsing. The procedure produces only a transient effect on rayons and cottons. A durable seroop can be imparted to cellulosic fabrics by finishing them with specially prepared emulsions of fatty alcohols, particularly oleyl, or fatty ethers or esters of ethylene glycol monobutyl ether (butyl Cellosolve).

Seroop finishes should be applied alone without adjuvants. The seroopy handle is totally destroyed by the addition of potent softening agents and is impaired by synthetic resin solutions and dispersions. Seroop finishes are popular on certain constructions of silk, such as taffetas, to produce a silk swish, and on tubular knit and pile fabrics derived from rayon and cotton.

**Wax Finishes.** Waxes (*q.v.*) and derivatives formed from them are water-repellent and glossy but too hard and brittle to be of service as softening agents. The waxy compounds are similar to oils and fats in that, when heated above their melting points, they orient themselves about fibers in much the same way.

The waxes most commonly used in textile finishing are the paraffins (see *Petroleum waxes*), beeswax, japan wax, and certain synthetic fatty amides of high molecular weight. Rosin (*q.v.*) and its hydrogenated or esterified derivatives are frequently grouped with the waxes in discussions of textile finishing. Waxes are usually applied to textiles in the form of emulsions, but the rosins are generally used as rosin soaps (see p. 897). The uses of wax emulsions in textile finishing are very diverse. They are generally employed with some other finishes or chemicals to produce some special finishing effect, but also, less commonly, alone.

Most of the nondurable types of water repellents are emulsions composed of waxes, usually paraffin wax, and either aluminum or zirconium salts (see *Waterproofing*). For the lustering and production of chintzes and embossed fabrics, wax-albumin or wax-casein mixtures (see p. 903) are used, and the elimination of yarn distortions in loosely constructed rayon or acetate fibers is accomplished by rosin soaps (see p. 897). Wax emulsions are valuable finishing adjuvants in many finishing formulations. Small amounts are often added to resin emulsions to plasticize the inherent stiffness of the resin and to supply a waxy touch. Rosin soaps act as extenders of starch in cotton

finishing and impart body and weight to acetate piece goods. One of the major uses of waxes in textile processing is in the finishing of sewing thread. The waxes, often fortified with a small amount of softening agent, are frequently the sole finishing agents employed in the production of this textile product. The wax is used to give a smooth lustrous surface, a compact structure, and maximum strength to the threads. Beeswax, paraffin waxes, synthetic waxes, and various blends of the three constitute most thread finishes.

#### DULLING AGENTS

It is desirable to reduce the luster of rayon so that it more closely resembles silk. The excessive brilliance of rayon materials can be subdued by the use of highly twisted yarns that break up light reflection, and by the deposition of pigment particles on the surfaces of the fibers. Rayon manufacturers accomplish the same effect in the manufacture of the fiber by means of pigments dispersed through the substance of the fibers themselves.

Structural correctives of luster are only applicable to certain types of fabrics such as crepes, and there are economic and functional objections to the use of dull yarns. Dull rayon yarns are serviceable only for the construction of lusterless fabrics, and they possess certain physical weaknesses. They are much lower in tensile strength than the bright yarns and more easily frayed and abraded by mechanical agencies.

The dulling of textiles is usually accomplished by the deposition of pigment particles on and within yarns and fabrics during finishing. The finishes which produce this pigment deposition are known as dulling agents. Dulling agents are essentially rayon finishes. They are occasionally used in silk finishing, less commonly in nylon, and only rarely on the newer hydrophobic fibers. Acetate is often dulled by special finishing procedures. Although dulling agents were originally developed to restrict only the excessive luster of rayon and mellow its appearance to that of silk, it was found that the appearance of rayon could be completely altered by delustering compounds and a range of effects secured, from a slight inhibition of luster to milky chalkiness.

The dulling of rayon may be accomplished in one of two ways:

(1) By alternately exposing fabrics to two solutions, the components of which react with each other to liberate dulling pigments within and upon the surfaces of the textile.

(2) By passing rayon goods through pigment dispersions. Instead of using actual dispersions, rayon is sometimes dulled with chemicals which are soluble under normal temperature conditions but decompose and form pigments during a subsequent drying operation.

It has been proposed that durable dulling effects be produced on rayon and acetate by etching the peripheries of the yarns by calcium thiocyanate and other chemicals. Such methods have met with little commercial success, as the strength and elasticity of the fibers are impaired by the treatment.

The earliest method of dulling rayon, and to a very limited extent silk, consisted in alternately exposing fabrics to solutions of barium chloride or hydroxide and sodium sulfate or zinc sulfate. Barium sulfate was formed and deposited on and within the fibers of the textile, thereby producing a dull appearance. The process is costly, presents manipulatory difficulties, and tends to produce spots and irregularities on

the surface of the finished material. This method has been replaced by pigment dispersions except in the case of knit goods, chiefly in the finishing of silk and rayon hosiery. Dulling agents are not applied to hosiery solely for the purpose of subduing excess luster, but rather to provide a multifunctional finish. The dulling agents, barium chloride and zinc sulfate, are applied with water repellents and softening agents to correct and mask knitting defects, "sleaze," and stitch irregularities.

Broad goods are usually dulled with pigment dispersions. Titanium dioxide, zinc oxide and sulfide, barium sulfate, zirconium dioxide, and clays are the pigments most generally used. Certain resinous pigments, highly polymerized urea-formaldehyde complexes and polystyrene and polymethacrylate resins are also receiving some use in the dulling of hosiery and delustering of hydrophobic fabrics. The pigments are usually dispersed in water with oils, glycol stearates, or other types of emulsifying agents and dispersants. The dispersant often contains a fixing or setting agent.

Titanium dioxide is the most effective dulling agent, having superior covering power. However, its high cost has stimulated the use of substitutes and extenders. The substitution of suitable qualities of clay and barium sulfate for a portion of the titanium dioxide actually aids in the production of more stable dispersions without substantially impairing dulling properties. Zinc compounds, which have been extensively used in dulling, usually give inferior results. Zinc oxide yellows during aging, and zinc sulfide frequently generates an obnoxious odor in use. Barium sulfate, zirconium dioxide, and the other dulling pigments occasionally used are not effective in producing complete delustering.

Both anionic and cationic pigment dispersants are used in dulling formulations. The cationic dispersants envelop the pigment particles and give them a positive electrical charge. They are, therefore, attracted to negatively charged fabrics and produce superior dullness and a softer handle. Fabrics dulled with cationic dulling agents are not durably delustered, and the pigment is removed more or less completely during the first laundering operation.

Wash-fast dulled rayons are difficult to produce. The pigment dispersions are used with durable film-forming finishes such as the cellulosic ethers and esters, latex emulsions, and emulsions containing polyvinyl acetate and polyacrylic acid esters. The results obtained by the joint application of pigment dispersions and resin emulsions to rayons have been disappointing in so far as obtaining wash-fast dulled fabric is concerned. Moreover, the film-forming finishes affect the handle of the goods. White pigments, such as titanium dioxide, cannot be successfully applied to fabrics dyed black or dark shades, as they impart an objectionable frosty appearance. The addition of rather high concentrations of sulfonated oils to the pigment dispersion tends to mask this frostiness but is not a very satisfactory corrective. Rayons dyed dark shades are usually dulled with clays, but only a small amount of delustering is thus obtained.

Acetate and the fabrics derived from hydrophobic fibers do not deluster satisfactorily by conventional rayon-processing procedures. There is poor attraction between such textiles and the dulling pigments. The surface deposits mark off and dust during use. Acetate may be permanently delustered by exposure to steam or boiling water, but it is difficult to secure a uniform dulling action by this procedure. More uniform dullness is secured on acetate fabrics by exposing them to soap-cresylic acid or soap-pine oil emulsions for several hours at 170–180°F. A loss of 30–50% of the strength of the fabric occurs during the dulling operation.

## WEIGHTING (See also p. 196)

The weighting of textiles is ordinarily detrimental. Only rarely does it improve the quality of fabrics; in most cases the serviceability of the merchandise and the fastness of the colors are reduced. Generally, weighting is not even intended to confer benefits to textiles and is used as a sales adjuvant, to simulate with inferior merchandise the handle and appearance of more costly material. This is usually accomplished by the use of finishing solutions containing body-building sizes such as modified starches and gums, softening and plasticizing agents to mellow the handle of the size, and hygroscopic agents and weighters. Fabrics are not so commonly weighted today as in the past. Few textiles are sold on the poundage basis, such sales being confined to certain types of knit goods and laces, novelty pile fabrics, yarns, and sundry items. Weighting is largely confined to these items, which are usually cotton and rayon.

Price is of prime consideration in the selection of the weighting agent, and those in most common use are urea, sodium sulfate, magnesium sulfate, potassium acetate, sodium acetate, glycerol, the glycols, and in special cases Rochelle salt. The concentration of weighting agent used in heavier finishes is usually quite high, and weighted fabrics are prone to develop adverse characteristics in the hands of the ultimate consumer. Among these may be listed "rain spots," white smears where the fabric is struck by water droplets, and excessive shrinkage during dry, cold weather. Cotton and rayon fabrics should not ordinarily be weighted more than 12-15%.

Urea is the most common weighting agent. It exerts a minimum effect on the fabric, and cellulosic fabrics weighted with it are comparatively resistant to the development of rain spots and white blotches. Since it stimulates the development of mildew and molds, it is usually applied with an antiseptic. Salt weighters, such as the sulfates and acetates, have somewhat better weighting properties than urea; they impart a somewhat stiffer handle, particularly in cold weather. The salts tend to impair the strength of fabrics during aging, and salt-weighted fabrics are inclined to develop rain spots. Barium sulfate is more troublesome to apply to fabrics than the soluble salts, as it is insoluble in water and must be used as a suspension; it also tends to dull the luster of fabrics and reduce the brilliance of colors. Glycerol, glucose, and the glycols are hygroscopic, and, although they impart soft, lofty handles to textiles and are without an adverse effect on fabrics, they must be used cautiously. Fabrics weighted with hygroscopic agents are prone to shrink in dry weather.

Rochelle salt (see *Tartaric acid*) is one of the most interesting of the weighting agents, although it is rather costly for simple weighting operations. It is one of the few weighting agents that enter into the intermicellar structure of cellulosic fibers to produce a semi-crush-retarding action. Borax, which is not commonly used as a weighting agent, has even more potent wrinkle-retarding properties.

## NONSLIP FINISHES

Broad goods composed of widely spaced continuous filament yarns have a tendency to become distorted in use. The yarns in such fabrics slip and slide on each other and exhibit a distortion of the woven structure so that the yarn distribution becomes uneven. Fabrics composed of easily distortable yarns are apt to fray at the edges when made into garments. Softening and lubricating agents accentuate the tendency of the yarns of a fabric to slip, whereas finishing sizes and drying agents have an inhibiting action.

Three types of nonslip correctives have been developed: (1) rosin or modified



rosins, usually in the form of soaps; (2) dispersions of polymerized urea- or melamine-formaldehyde resins; (3) pigment dispersions.

The most favored type of slip retardants are partially saponified rosins, the so-called rosin soap, to which a small amount of a softening agent is added to produce more pliable films. Such finishes cement the yarns of a fabric together at their points of contact, thereby producing a fixed yarn structure. The finish is generally applied to textiles from a jig or quetsch, followed by mechanically treating the fabric in the conventional manner. To improve the wash resistance of the finish, fabrics are often submerged in a metallic salt solution after the rosin application. Although pigment and resin dispersions often act as excellent slip retardants, they are less commonly used in textile processing as they tend to impair the luster of continuous filament yarns.

#### DYE CORRECTIVES

Dyeing and finishing may be regarded as complementary operations by which a textile is perfected for final consumption. The finishing operation should in no way deface the results of the dyer's art, and the dyeing operation should leave a textile in a condition to acquire and retain finishes. Actually the two operations supplement each other, and finishes are used to mask and correct weaknesses in color as well as those of the textile itself.

Two general dye weaknesses minimizable by finishing are: (1) imperfect fixation of color onto fabrics and (2) lack of fastness of dyes to atmospheric and laundering agencies.

Imperfect fixation of dyes onto textiles is an occasional result of existing dyeing procedures. It may be caused by a low affinity of the color for a fabric, adverse conditions of dyeing, or inadequate rinsing to remove excess color. Textiles on which the dyes are inadequately affixed crock (colors rub off) and bleed (stain water and perspiration) and as a consequence tend to smear and tint objects which impinge against them in use, particularly damp substances. Crocking and bleeding may be either accentuated or restricted by the finishing operation. Mechanical finishing processes such as steaming and dampening may have either a corrective or an adverse effect, depending upon whether the defect is due to an incomplete color fixation or to lack of affinity of the textile for the dye. Steam usually induces a better dye-to-fabric union, but it occasionally lowers the ability of a fabric to bond color. Of the finishes most generally used in textile finishing, oils, fat and waxes increase the tendency of dyes to crock; conversely the film-forming sizes and resins restrict it. Although no general inhibitors of crocking and bleeding have been developed, correctives are in use that act as specifics in setting certain colors or even classes of colors. Formaldehyde and its urea and melamine resins often act as dye-setting agents; glyoxal and some of its derivatives are still more potent.

The dyes most amenable to fixation are the direct colors. These may be set into fabric by cationic surfactants and heavy-metal salts; the correctives form insoluble compounds with free direct colors which are affixed, at least temporarily, to the surface of a textile. The cationic softening agents are particularly effective as they accomplish the dual function of setting loose colors and softening the textile. Similarly, color fixation can be obtained with the salts of heavy metals. Zinc, magnesium, and aluminum salts are particularly effective as they form colorless ions, and in the forms of their acetates and formates do not appreciably deteriorate fabrics. The salts of such metals are not commonly used alone but usually with a surface-active agent such as a fatty

alcohol sulfate, which aids wetting and prevents the formation of insoluble conglomerates. Water repellents containing paraffin wax and aluminum salts are very effective in setting direct colors.

Most of the color fixatives have a transient action, and few remain on a material after a single laundering. Direct colors are not particularly fast to washing. Certain auxiliaries form very insoluble complexes with direct colors and are useful not only in reducing crocking and bleeding but also in increasing the wash-fastness of textiles dyed with such dyes. Such finishes are usually high-molecular-weight condensates of formaldehyde and nitrogenous bases: melamine, guanidine, or dicyanodiamide containing copper chloride.

Dyes, and even textiles themselves, are faded and deteriorated by weathering and sunlight. It is believed that the degradation is an oxidation catalyzed by actinic rays from the sun, but the subject has not been extensively studied. It has been observed that certain finishing agents such as the titanium dioxides of dulling agents and the "tin" in tin-weighted silk accentuate the deterioration of dyes and fibers, whereas certain film-forming finishes restrict it. Sun-protective finishes are used on fabrics from which awnings, tents, and outdoor furniture are made. Cellulose acetate and polyvinyl acetate are particularly effective in protecting fabrics against weathering.

The colors employed in dyeing acetate are very susceptible to change by atmospheric agencies. Unlike most fading phenomena, the change is due less to oxidation than to minute traces of impurities in the air, oxides of nitrogen, and sulfurous vapors. The fading is inhibited by the presence of alkaline finishes on the surfaces of the textile. The fume retardants formerly employed were simple amines, and salts such as sodium borate. Such finishes are very soluble in water and have only a transient color protective action. This class of finishes has been largely replaced by certain types of aromatic and alkylated aryl amines which are substantive to acetate and are not removed by conventional laundering and dry-cleaning procedures. Diphenylethylenediamine and other diaryl- and alkaryl-substituted alkylenediamines are often used to make dyed acetate yarns and fabrics fume-resistant.

#### MILDEW- AND ROT-RESISTANT FINISHES

Some textile products will normally be exposed to moisture and warmth, the factors favorable to the development of fungi and bacteria. Canvas for hosepipes, tent cloth, awnings, screens, coverings for outdoor furniture, fish lines and nets, because of the conditions of their use, are particularly subject to deterioration by microorganisms. In addition to the coarser textile materials mentioned above, large quantities of medium and fine fabrics of cotton and linen are stored and transported under conditions which may give rise to mildew, and similar considerations apply to yarns and raw fibers.

Microorganisms vitiate the quality of textile products by forming unsightly green deposits over their surfaces (mildew) and by actual destruction of the textile substance (rot). A great difference exists in the susceptibility of fibers to deterioration by fungi and bacteria. The only two classes in which rot and mildew are problems of industrial interest are the cellulosic and the woolen fibers. Bacteria do not normally develop on silk, and the molds which do attack silk attack only silk gum (sericin). Cellulose acetate and the hydrophobic fibers are immune to microorganisms.

Unfortunately for the textile manufacturer, most of the textile products fabricated for materials to be used under conditions favoring the growth of rot and mildew are

derived from cotton and bast fibers. Consequently, immunizing finishes are confined almost exclusively to the finishing of cellulosic fibers. Comparatively few chemicals are serviceable for this purpose. Only a few have the requisite affinity for cotton and rayon fabrics and the low toxicity, lack of color and odor, and low volatility to be of interest in textile finishing. Moreover, suitable antiseptics must not be expensive. *The antiseptics most generally used for mildew-resisting fabrics are:*

(1) Organic compounds—halogenated and phenylated phenols (Dowicides); bis(2-hydroxy-5-chlorophenyl)methane (G4); salicylanilide.

(2) Organometallic derivatives—copper naphthenates; cadmium soaps; and phenyl mercurials.

(3) Inorganic compounds—zinc chloride; cuprammonium compounds.

Antiseptic finishes are used chiefly to protect quality cotton and linen fabrics, and especially those that contain starch and sizes, against the development of molds and mildew during storage and transportation and to inhibit the development of decay and rot on coarse textiles exposed to weathering.

The immunization of fabrics against mildew and rot during storage is a relatively simple operation. It was formerly secured by passage of a textile through a zinc chloride solution. Zinc chloride has in recent years been replaced by the more potent organic antiseptics, the halogenated and phenylated phenols, and salicylanilides. These agents are readily removed from fabrics by laundering and dry cleaning or even by water leaching, but they may be durably affixed to textiles by conversion to their lead salts. This is accomplished by passing fabrics impregnated with the antiseptic through basic lead acetate solutions of adequate concentration. Such a procedure has proved effective in weatherproofing awnings and outdoor furniture. The mercurials and quaternary ammonium compounds have been proposed for the same purpose but are little used commercially.

The rot resistance of heavy, coarse textiles such as tents and fire hoses is of much industrial importance. Most of such processes involve the use of copper in one form or another. Metallic compounds containing copper are cheap and efficient and in addition render treated fabrics immune to termites and cellulose-eating insects. The copper is usually applied in the form of its cuprammonium salts for general antiseptic use, as copper oleate in various water-repellent compositions, as copper naphthenates in solvent preparations, and with bitumen in coatings.

### External-Internal Finishes

All fabrics possess inherent weaknesses of structure and properties that restrict their utility for certain purposes. The defects may be circumvented by corrective finishes that alter the physical or chemical characteristics of the textiles. The alteration may occur on the peripheries of the fibers, or in their internal micellar structure, or both. Such finishes may be referred to as external-internal finishes but more commonly as corrective finishes. The most important corrective finishes are those used for dimensional control, water repellency, fire retardancy, and moth inhibition.

### DIMENSIONAL CONTROL

*One of the most common and serious weaknesses of textile fabrics is their tendency to shrink during laundering, and stretch or elongate in use. There are two causes of shrinkage; one is an unavoidable condition of yarn and fabric manufacture, the other*

an inherent defect of the filaments themselves. Considerable tension is imposed upon yarns and fabrics during their preparation and during dyeing and finishing operations. The tension results in an excess stretch which produces an unstable yarn and fabric structure. In many cases deliberate stretching is applied to materials to secure maximum linear and lateral yardage. It is often assumed that shrinkage is the result of a release of the tensions and extensions produced during the process of cloth manufacture; in other words, water acts as a medium causing the micelles, fibers, and yarns to contract to the position of minimum strain from which they were stretched during spinning and weaving. Such shrinkage is known as relaxation shrinkage and constitutes the major amount of that produced in the laundering of fabrics composed of acetate rayon and the hydrophobic fibers.

The major cause of the shrinkage of textiles derived from the natural fibers and the viscose rayons is alteration in the internal structure of their filaments induced by water. Rayon, as well as cotton and most other natural fibers, swells in water. The swelling is the result of a passage of water into the inner structures of their fibers and a resulting rearrangement of the micellar attachments. Such a rearrangement results in linear contraction or fiber shrinkage. The shrinkage of wool differs from that of all other textile fibers in that there are two mechanisms, relaxation and felting (see "Predyeing Operations"; *Wool*).

The dimensional control of fabrics (shrink-resisting) is accomplished by either mechanical, chemical, or physicochemical means. Cotton goods are usually rendered shrink-resistant by preshrinkage and mechanical compressive shrinkage procedures. The dimensional structure of the hydrophobic fabrics is secured by stretching the materials to fixed dimensions and setting this structure with heat and steam. This pre-setting operation causes a rearrangement of the micelles within the hydrophobic fibers to produce a stable filament structure.

Wool and rayon fabrics are not ordinarily rendered shrink-resistant by mechanical means. Relaxation shrinkage in wool fabrics can be prevented by setting with hot water or steam. Alternatively, the fabric may be relaxed by "London shrinking," which consists in moistening it well and allowing it to dry slowly in the absence of restraint.

**Shrink-Resistant Woolens.** Most shrink-resistant wool processes achieve their objective by dissolving in whole or part the serrations from the wool fiber or in otherwise modifying or filling the intrascale spaces. Two general methods exist: chemical processes which partially dissolve and modify the peripheral structure, and resinous finishes which act partly by mashing the fiber scales, and partly by "spot welding" the fibers together, thus preventing their movement.

Many chemicals are effective in modifying the scale structure. These include chlorine in one form or another, bromine, proteolytic enzymes such as papain, and alcoholic solutions of caustic soda or potash. Chlorination is most commonly resorted to to produce shrink-resistant wool. The wear resistance of chlorinated fabrics is less than that of resin-treated fabrics.

Wool is also rendered nonfelting by a number of resinous materials, including monomeric methyl methacrylate applied to wet wool in the form of a vapor, solvent solutions of anhydrocarboxyglycine(2,5-oxazolidinedione) and the methylated methylolmelamines. The only resins to have achieved much commercial success in shrink-retarding wool are the alkylated methylolmelamines.

These resins are applied to wool with an acid catalyst such as formic acid from an

aqueous solution, after which the impregnated wool is dried and cured for a few minutes at 300°F. Alkylated melamine-formaldehyde condensates, for reasons not very thoroughly understood, appear to anchor themselves and accumulate at the interstices of the scales where the greatest corrective action is exerted. Other melamine- and urea-formaldehyde resins inhibit wool shrinkage but are not effective enough to be of commercial interest.

**Shrink-Resistant Rayon.** Rayon fabrics, particularly those derived from spun yarns, are more dependent upon chemical finishes to secure dimensional control than any other textile material. Rayons are very susceptible to shrinkage and in addition elongate and become distorted in use. Rayon cloth, unlike cotton, is not amenable to mechanical shrinkage processes. The compressive shrinkage methods, used so successfully on cotton goods, leave rayons elastic and distorted.

The correctives used for the dimensional control of rayon are the urea and melamine resins or their equivalents. These finishes not only inhibit shrinkage but also minimize the stretch and elongation that heavy rayon fabrics undergo in use. The discovery that these adverse factors could be corrected by resins was of great importance to producers of spun rayon fabrics. Prior to the discovery, rayon had not been commonly used in the fabrication of heavier apparel such as women's coats and suits and men's sportswear and tropicals. Nearly all varieties of urea- and melamine-formaldehyde resins are serviceable for dimensionally controlling rayon fabrics. This is surprising, as a fundamental difference exists in the distribution of resins of different degrees of polymerization on rayon fibers. The resin monomers and low polymers are deposited within the filaments, whereas the more highly polymerized products coat the fibers as an external finish.

The mechanism of dimensionally controlling rayon by urea-formaldehyde resins is still uncertain. It is believed to be due to an alteration in the intermicellar structure of rayon fibers. The micellar structure of rayon possesses inherent weaknesses, as it contains free hydroxyl groups and rather feeble crosslinkages between the micelles. Shrinkage is primarily due to the free hydroxyl radicals. The radicals adsorb water, which swells the fibers. This results in breaks in the intramicellar crosslinkages and, upon removal of the water, leads to contraction, new micellar attachments, and linear shrinkage. The elongation of rayon in use is believed to be due to the weaknesses in the intramicellar crosslinks.

Urea- and melamine-formaldehyde resins, through the medium of free methylol groups in the condensates, react with the free hydroxyl radicals in the micelles to block their swelling action, while the crosslinkages are stabilized against break by reactive groups in the resins. It is easy to understand how this may be accomplished by internally deposited resins but more difficult with external coatings. It is believed that external resin finishes accomplish the same function as the internal finishes by means of resin sidechains that penetrate the pores of the peripheral fiber wall and react with the hydroxyl and other reactive groups in the micellar structure. Urea- and melamine-formaldehyde resins are generally applied to rayon fabrics from an aqueous solution containing a catalyst and a softening agent. The impregnated fabric is then dried and subsequently cured for a few minutes at 300°F. The catalysts used to set the correctives are ammonium phosphate, sulfate, chloride, or thiocyanate, zinc chloride, and other mildly acidic compounds.

Although urea- and melamine-formaldehyde condensates or their equivalents are almost a necessity in finishing certain types of rayon, they are far from a finishing

panacea and impart so many defects to cellulosic fabrics that their eventual replacement is inevitable. Rayons dimensionally controlled with existing types of resin gradually lose their shrink-inhibition upon repeated laundering, tend to develop malodors during storage, are often tender and brittle, are cut by needles during sewing, and adsorb chlorine from the hypochlorite bleach bath. However, the dimensional control properties initially imparted to rayon fabrics by the urea and melamine resins are so superior that this acquired characteristic overbalances in importance the defects simultaneously developed. By using proper methods of application and resin correctives the rayon defects induced by resin finishing can be minimized.

The fishy odors occasionally observed on dimensionally controlled rayon are due to amines generated from the resins during drying and curing. The formation of such amines may be inhibited by the use of urea or dicyandiamide and the employment of nonammoniacal catalysts. As additional security against a possible development of odors, most textiles finished with urea-formaldehyde condensates are given a light scour after curing to remove amines and amine precursors.

The adverse physical effects imposed on rayon by the dimensional control resins are generally circumvented by softening and lubricating agents. Substantive softening agents are most generally used for this purpose. Dispersed silicone emulsions have also proved effective and, in addition, impart water-repellent properties to the fabric.

It is difficult to correct the tendency of either urea- or melamine-formaldehyde resins to retain chlorine from the hypochlorite bleach bath. Chlorine so combined is gradually liberated as hydrochloric acid during aging and has a very inimical effect on cellulosic materials.

Improved methods of dimensionally controlling rayon fabrics have been developed recently. These employ such resins as the cyclic alkylurea-formaldehyde condensates, the hydroxyethyl cellulose-formaldehyde complexes, and glyoxal or its resinous derivative, "tetramethylol acetylene diurea," formed from urea, glyoxal, and formaldehyde.

Cyclic alkylurea-formaldehyde condensates inhibit the shrinkage of rayon fabrics as effectively as the conventional urea-formaldehyde resin, have a much lower chlorine retentive value, and impart to fabrics a much softer handle and greater pliability. The condensates are applied to fabrics in which low chlorine retention and a soft handle are of paramount importance.

The most effective method of shrink-retarding rayon fabrics, however, involves the use of the hydroxyethyl cellulose-formaldehyde complexes. These resins are devoid of chlorine adsorptive properties, do not impart a malodor to fabrics during aging, and inhibit shrinkage throughout the normal life of a material. In addition, the complexes protect fabrics against mechanical abrasive agencies. The complexes are applied to rayons with a zinc or ammonium nitrate catalyst and affixed to the fabrics at a temperature of 150°C. Rayons finished with hydroxyethyl cellulose-formaldehyde complexes have a harsh handle that has restricted their applications.

Glyoxal (see *Glycols*) and its derivative, tetramethylol acetylene diurea, are assuming importance in shrink-retarding rayon fabrics ("Sanforset" process). When properly affixed to rayon fabrics, these substances durably control rayon against dimensional change and impart to the finished fabric a soft handle. The glyoxal and tetramethylol acetylene diurea are generally applied to fabrics in the presence of high concentrations of sodium bisulfate and Glauber's salt, after which the rayon is dried and baked for a few minutes at 150°C. Subsequent to baking, the textile should be

washed for a few minutes in dilute soap solution to remove excess acidity and possible progenitors of odor.

#### DURABLE GLAZED CHINTZ EFFECTS

Although the urea-formaldehyde resins are probably the most versatile of chemical finishing agents, none of the innovations they have produced in textile processing is as surprising as the fact that they impart a durable chintz effect to cellulosic fabrics. Sheen has always been a desirable fabric characteristic, and surface luster is particularly esteemed on certain types of decorative material. Surface sheen, or chintz, was formerly imparted to cotton goods by films of wax, sometimes wax-albumin, polished to a high luster on hot friction calenders. The effect was due to a surface film; it was transient and survived only the first laundering or dry cleaning. The use of chintzes has been expanded by the development of durable types based on urea-formaldehyde monomer and polymers.

A durable chintz is usually obtained by passing cotton goods, less commonly rayon fabrics, through a solution containing 5–20% of dimethylolurea or a low-polymer urea-formaldehyde resin and a catalyst. Casein, wax dispersions, pigments, and other auxiliaries are frequently added to the resin solution to produce certain effects. The impregnated fabric is dried and subsequently lustered by passing the textile over friction calender rolls.

The type of polymer used to produce chintz effects depends on the handle requirements of the finished textile. Softer, more pliable chintzes are produced by the use of the lower polymers. The more highly polymerized resins produce a more heavily bodied, stiffer material. Occasionally waxes, gums, starches, and even albumin are added to a chintz finishing bath to produce special effects.

Sulfonated oils or an equivalent are invariably present in the finishing bath to prevent the sized fabric from sticking to the calender rolls.

#### MOTHPROOFING OF WOOL

Textiles are relatively immune to insect pests, but a few exceptions exist. Rayons are attacked, particularly in the deep south and the tropics, by "silver-fish," and wool is eaten by the larvae of several species of moths and by the carpet beetle. The damage wrought by these insects is considerable. It is estimated that annual losses in excess of two hundred million dollars result from the depredations of moths on wool in the U.S., yet wool is not commonly mothproofed in America. In certain parts of Europe, particularly in the Scandinavian countries, the mothproofing of wool is almost a standard finishing procedure.

Wool is readily immunized against moth damage by suitable chemical finishes. Many chemicals are capable of rendering wool moth-repellent. Almost any potent antiseptic, soluble heavy metal salt, or toxic nonvolatile organic derivatives are capable of affording wool protection. Even certain dyes, such as Marius Yellow, and some of the alkylated arenesulfonates are effective inhibitors. Most of these possess other characteristics that contraindicate their use as wool finishes.

The most commonly used moth repellents are the inorganic and organic fluosilicates, the triphenylmethanes or equivalents, the phosphonium compounds, and the insecticide DDT. In addition, wool may be rendered moth-repellent by alterations in the chemical structure of its fibers.

The triphenylmethanes and the triphenylphosphines are the most effective of the existing moth inhibitors, as they are effective throughout the normal life of a fabric.

The fluosilicates are more commonly used in the U.S. as they are lower in price, present few problems in finishing, and perform sufficiently well to meet present-day protective requirements. Sodium, magnesium, or ammonium fluosilicates are commonly used; double sodium aluminum fluosilicates are also used. The fluosilicates have little effect on the strength and elasticity of woolen fibers. They do, however, harshen the handle of wool. A somewhat softer handle can be secured by the use of certain triethanolamine and other organic fluosilicates. Fluosilicates are applied to wool by passing the textile through aqueous solutions of the proofing agent. Wool containing  $\frac{1}{4}$  % fluorine in the form of fluosilicate is immune to moth damage. The protective action is not durable and is destroyed during the first laundering operation.

The ideal corrective finish, one which will accomplish its objective without altering the physical and chemical properties of the textile processed, has been found in the mothproofing of wool with certain triphenylmethane derivatives. These are structurally similar to acid colors and are applied to wool in a similar manner. They are generally referred to as colorless dyes. The fixation of the triphenylmethanes onto wool is accomplished by immersing the textile in a solution containing the proofing agent, an acid, and a wetting agent and heating the liquor to boiling. Wool so treated is durably immunized against moth damage. The effect is not impaired by laundering, dry cleaning, sunlight, or any of the processing or wear conditions to which wool is normally subjected. About 3% of proofing agent on the weight of the wool is required to secure a satisfactory proof. Typical triphenylmethane derivatives used in mothproofing are condensates of *o*-sulfobenzaldehyde and 2,4-dichlorophenol (Eulan New), *p*-chlorosulfobenzaldehyde and 2,4-dichlorophenol (Eulan CN Extra), and Mitin FF (see *Triphenylmethane dyes*).

The phosphonium compounds are not as effective moth inhibitors as the colorless dyes. The advantages of the phosphoniums lie in the simplicity of their applications to wool and the fact that, when once affixed to wool, the textile has sufficient durability for many conditions of use. The phosphonium is usually applied to wool at a bath temperature of 40–50°C. Wool containing about 3% of its weight as triphenyl(3,4-dichlorobenzyl)phosphonium chloride is immunized against moth damage.

DDT possesses little affinity for wool, but it is such an effective insecticide that only very small quantities are needed. DDT is generally applied to wool in the form of a cationic emulsion. Small amounts of melamine and coumarone resins are generally present in the emulsion in order to increase the resistance of the insecticide to removal from wool by washing and dry cleaning. The results have not been very satisfactory, and DDT must be classified as a nondurable moth repellent for wool.

One of the latest methods of mothproofing wool is to modify the keratin structure by chemical methods. This is accomplished by breaking the disulfide linkages of wool. The modified wool is resistant to moth damage.

### Internal Finishes

Internal finishes are those deposited within the substance of a textile fiber. The finishes are used chiefly as correctives to inhibit some inherent weakness in the structure of fibers. Many durable waterproofing agents and fire retardants are of this



type. Internal finishing is confined to textiles composed of the hydrophilic fibers.

#### CRUSH-RESISTANT FINISHES

Although cotton and rayon fabrics are the most important textile fibers from a volume standpoint, they possess inherent weaknesses that have tended to exclude them from the field of luxury merchandise. One defect is their tendency to crush and wrinkle easily. The defects are believed due to a faulty intrafiber structure which is capable of correction by dimethylolurea, certain aldehyde-formaldehyde monomers, or even formaldehyde itself. The correction of the faulty structure is facilitated by the porous peripheral wall and loose internal structure of both rayon and cotton, which permits easy ingress of the correctives through the wall to the points of fiber weakness. The inhibition of creasing, however, is only barely possible, as the surface orifices are just large enough to permit the entrance of dimethylolurea.

The mechanism by which wrinkle resistance is secured in cellulosic fabrics has not been definitely established. It is believed that the resin monomers alter the internal structures of the cellulose chains within the filaments, possibly by the formation of methylene crosslinkages or bridges. In any event, the monomers are polymerized within the fibers by acidic catalysts and the polymer is deposited as an internal finish.

The finishing agent generally used to impart wrinkle resistance to cellulosic fabrics is dimethylolurea. It is usually applied with an acidic catalyst to set or affix the monomer to the inner structures of the fibers as a resin. The catalysts usually employed are ammonium and amine salts and certain other inorganic salts such as zinc chloride. Urea and dicyanodiamide are frequently added to the resin to inhibit its tendency to form malodors.

Optimum crush-resistant properties are obtained with cellulosic fabrics by the adherence to prescribed methods of application. The apertures on the peripheries of cotton and rayon fabrics are just large enough to permit the entrance of dimethylolurea molecules, and any method of application, such as tension, that produces a partial closure of these orifices results in an external formation of resin. Such a deposit is without value in the production of wrinkle resistance.

Wrinkle-resistant fabrics are generally obtained by impregnating fabrics in a relaxed condition with a finishing solution containing dimethylolurea, a catalyst, and urea or dicyanodiamide, and drying and curing the sized materials under just sufficient tension to prevent the formation of wrinkles. After curing, the fabrics are washed to remove externally formed resins and also impurities which develop odors during aging. Although dimethylolurea imparts crush-resistant properties and an excellent handle to cellulosic fabrics, this is accomplished at the sacrifice of some tensile strength and an impairment in the wearing qualities of the treated material. The amount of resin required to impart crush resistance to fabrics varies with the type of material and its construction. Substantially the same order of wrinkle resistance may be realized with much less resin in cotton than in rayon. It is not generally customary to use more than 7% resin on cotton, but to produce the same effect on linen, filament rayon, and spun rayon fabrics a resin content of 10, 12½, and 17½%, respectively, is required.

Although many alternatives have been proposed for dimethylolurea as crush-resisting agents, only the melamine-formaldehyde monomers, the cyclic alkyl urea-formaldehyde condensates, and formaldehyde have achieved commercial success. All are applied to fabrics in much the same way as dimethylolurea and require similar

processing conditions. The melamine-formaldehyde precondensates are extensively used on cotton goods to impart wrinkle resistance. Substantially lesser amounts of resin are required to produce crush inhibition, and the processed fabrics are alleged to possess wearing qualities superior to those rendered wrinkle-resistant with dimethylolurea. The chief advantage of the cyclic alkylurea-formaldehyde monomers over competitive crush inhibitors is that merchandise inhibited with this resin is comparatively resistant to chlorine retention. Although formaldehyde is an effective wrinkle retarder, it is not extensively used for that purpose in textile finishing, as it too severely impairs the wearing properties of the processed fabric. It is used chiefly in the production of crush-resistant velvets and pile fabrics.

Certain inorganic salts are also capable of giving crease-resisting characteristics to rayons and cottons. Compounds such as the borates, silicates, and stannates are particularly effective, but treated fabrics have at least two disadvantages compared with those containing urea-formaldehyde resins. First, the crease-resisting effect is broken down by repeated crumpling and squeezing and, secondly, the effect is not sufficiently fast to washing.

#### WEIGHTING

Internal weighting, which involves the deposition of pigments or chemicals in the inner structure of fibers solely for the purpose of imparting body and weight, is, like external weighting, a detrimental practice that cannot be too strongly condemned. Such weighting is confined chiefly to silk. Silk exhibits a remarkable affinity for metallic salts. Such salts enter the inner structure of silk without substantially altering the appearance or inherent softness of the textile; the weighting agents simply supply body and weight. Most weighting agents catalyze the susceptibility of silk to deterioration by sunlight and atmospheric agents and greatly impair its utility.

Silk is usually weighted by the tin-phosphate-silicate process. This consists in alternately exposing boiled-off silk to solution of stannic chloride and sodium phosphate, usually a mixture of mono- and diphosphates, adjusted to a pH of 8. Several passes of the silk are made through the tin and phosphate liquors. A subsequent treatment in a sodium silicate solution adds more weight to the fabric. By this process it is easy to weight silk 60% or more. The operation improves the draping qualities of light silk constructions but at a considerable sacrifice of serviceability.

Rayon and even cotton may be similarly weighted, but the practice has not received much industrial consideration. The tin is not so readily affixed to the cellulosic fibers as to silk, and much is removed from the fibers during ordinary washing. Moreover, cellulosic fabrics are not costly enough to make tin adulterations attractive.

#### Bibliography

- American Viscose Corp., *Rayon Technology*, McGraw-Hill, N.Y., 1948.  
Charlesworth, H., and associates, *Textile Machinery*, Mapleton House, Brooklyn, N.Y., 1947.  
Clark, G. W. A., *Clark's Weave Room Calculations*, 3rd ed., Clark Publishing Co., Atlanta, 1949.  
*Dictionary of Textile Terms*, 4th ed., Dan River Mills, Danville, Va., 1947.  
Herbig, W., *Die Oele und Fette in der Textilindustrie*, Stuttgart, 1923.  
Greenwood, Henry, *Handbook of Weaving and Manufacturing*, 2nd ed., Pitman, 1948.  
McCutcheon, J. W., *Synthetic Detergents*, MacNair-Dorland Co., N.Y., 1950.  
Mantell, C. L., *The Water Soluble Gums*, Reinhold, N.Y., 1947.  
Mauersberger, H. R., *American Handbook of Synthetic Textiles*, Textile Book Publishers, N.Y., 1952.  
Mauersberger, H. R., and Schwarz, E. W. K., *Rayon and Staple Fiber Handbook*, 3rd ed., Rayon Handbook Co., N.Y., 1939.

- Merrill, G., Macormac, A. R., and Mauersberger, H. R., *American Cotton Handbook*, 2nd ed., Textile Book Publishers, N.Y., 1949.
- Schaeffer, Albert, *Action of Alkali on Cellulose*, Hobart Publishing Co., Washington, D.C., 1948.
- Schwarz, A. M., and Perry, J. W., *Surface Active Agents*, Interscience, N.Y.-London, 1949.
- Shinn, W. E., *Principles of Knitting*, Vols. I and II, Clark Publishing Co., 1946, 1949.
- Silcox, A. E., and Landau, A. L., *Slashers and Slashing*, Fiber Publishing Co., 1950.
- Siu, R. G. H., *Microbial Deterioration of Cellulose*, Reinhold, N.Y., 1951.
- Speakman, J. B., and Chamberlain, N. H., "Emulsions and Emulsification in the Wool Textile Industry," in *Emulsion Technology*, Chemical Pub. Co., N.Y., 1943.
- Speel, H. C., *Textile Chemicals and Auxiliaries*, Reinhold, N.Y., 1952.
- Textile Foundation Reports.
- Textile World's Flow Charts, "Cotton" (Jan. 1947); "Knitting" (April 1947); "Wool" (August 1947); "Continuous Filament" (March 1948); "Felt" (March 1949); McGraw-Hill Publishing Co., New York.
- Von Bergen, W., and Mauersberger, H. R., *American Wool Handbook*, 2nd ed., Textile Book Publishers, N.Y., 1948.

#### LEADING TEXTILE JOURNALS (Chiefly American and British)

- |                                                                                           |                                                         |
|-------------------------------------------------------------------------------------------|---------------------------------------------------------|
| <i>America's Textile Reporter</i><br>(formerly <i>American Wool and Cotton Reporter</i> ) | <i>Modern Textiles Magazine</i>                         |
| <i>American Dyestuff Reporter</i><br>(official journal of the A.A.T.C.C.)                 | <i>Mondo tessile</i>                                    |
| <i>A.S.T.M. Standards on Textile Materials</i>                                            | <i>National Cleaner &amp; Dyer</i>                      |
| <i>British Rayon &amp; Silk Journal</i>                                                   | Papers of American Association of Textile Technologists |
| <i>Bulletin de l'institut textile de France</i>                                           | <i>Rayon and Synthetic Textiles</i>                     |
| <i>Bulletin of Lowell Textile Institute</i>                                               | <i>Rayonne et fibres synthétiques</i>                   |
| <i>Canadian Textile Journal</i>                                                           | <i>Rayon, Zellwolle und Chemiefasern</i>                |
| <i>Deutsche Textilgewerbe</i>                                                             | <i>Skinner's Silk &amp; Rayon Record</i>                |
| <i>Dyer, Textile Printer, Bleacher and Finisher</i>                                       | <i>Textile Age</i>                                      |
| <i>Fibres, Natural and Synthetic</i>                                                      | <i>Textile Bulletin</i>                                 |
| <i>Hosiery Times</i>                                                                      | <i>Textile Forum</i>                                    |
| <i>Hosiery &amp; Underwear Review</i>                                                     | <i>Textile Industries</i>                               |
| <i>Indian Textile Journal</i>                                                             | <i>Textile Industries and Fibers</i>                    |
| <i>Industrie textile</i>                                                                  | <i>Textile Journal of Australia</i>                     |
| <i>Journal of the Oil &amp; Colour Chemists' Association</i>                              | <i>Textile Manufacturer</i>                             |
| <i>Journal of the Society of Dyers and Colourists</i>                                     | <i>Textile Mercury and Argus</i>                        |
| <i>Journal of the Textile Institute</i>                                                   | <i>Textile Recorder</i>                                 |
| <i>Knitter</i>                                                                            | <i>Textile Research Journal</i>                         |
| <i>Melliand Textilberichte</i>                                                            | <i>Textile World</i>                                    |
|                                                                                           | <i>Textil-Praxis</i>                                    |
|                                                                                           | <i>Zeitschrift für Textil-Industrie</i>                 |

H. C. SPEEL AND H. H. MOSHER

## TEXTILE TESTING

Physical testing of textiles includes measurement of: (1) "inherent" or "intrinsic" fiber properties; (2) the properties of fiber aggregates either as bulk fiber (for example, batting) or as yarns; (3) the properties of fiber and/or yarn aggregates as they exist in woven fabrics, or felts; and (4) the relationships that exist between fiber, yarn, and fabric. Thus the performance of any textile structure is dependent upon a combination of inherent fiber properties, as well as upon the geometrical arrangement of fibers in yarns and of yarns in fabrics. See also *Fibers; Textile technology*; and articles on the fiber materials, such as *Cotton; Linen; Polyamides; Protein fibers, synthetic; Rayon and acetate fibers; Silk; Textile fibers, synthetic*; and *Wool*.

According to Hamburger, Platt, and Ross (33) fiber properties are governed by:

- I. Polymer properties.
- II. Geometric modifiers:
  - A. Orientation of chain molecules with respect to fiber axis.
  - B. Cross-sectional area and shape.
  - C. Length.
  - D. Crimp.
  - E. Surface contour.

Yarn properties are determined by:

- I. Fiber properties.
- II. Geometric modifiers.
  - A. Fineness.
  - B. Twist.
  - C. Cross section.
    - 1. Diameter
    - 2. Compactness.
  - D. Surface character.

Fabric properties are determined by:

- I. Yarn properties.
- II. Geometric modifiers.
  - A. Tension on yarn components.
    - 1. Tension on elements in weaving process.
    - 2. Compactness of weave.
  - B. Design.

It follows that any physical or chemical treatment which alters fiber or yarn property will produce a consequential change in fabric property. Furthermore, certain "wet finishing" treatments can often modify a fabric far more extensively than geometric methods. This is why textile finishing (*see Textile technology*) is such an important science and art.

Textile tests may also be grouped into those that are nondestructive in nature and those that are either partly or wholly destructive. Nondestructive tests include such measurements as length, diameter, weight, cross-sectional area, and refractive index. Destructive tests include measurements of tensile elastic behavior, effect of chemicals, heat, aging, dielectric properties, and the like in which the tests cause a permanent change in the property.

Most of the following discusses the interpretation and evaluation of textile properties from the engineering standpoint. For details of test methods or specifications see references 1,3,39,81.

### Fiber Properties

**Length.** With the exception of silk, all natural fibers must be spun into yarns in order to serve as useful textile materials. Silk and the synthetic fibers may be utilized in continuous filament form or cut up into selected short lengths (staple), 1 in. to as long as 15 in., and then spun into yarns. One criterion of yarn performance is the staple length of the fiber employed. In cotton, the longer the staple length, the better is the quality. The staple length is prepared by laying out a uniform array of fibers of progressive lengths from the longest to the shortest. Both the average or mean staple length and the distribution of fiber lengths are calculated. See reference 3 for details regarding wool, cotton, and other fibers.

**Diameter.** Fiber softness or flexibility is a function of diameter, and "fineness" or "quality" is particularly significant for cotton and wool fibers.

The quality of wool is determined on a statistical basis of distribution of fiber diameter measured with the microscope. Again, both the mean value and distribution around the mean are measured (3). Wool is thus classified into many grades of quality. For example, a 64's wool has a mean diameter range of 21.1–22.4  $\mu$ , while not more than 6% of the fibers exceed 40 microns in diameter.

The fineness of cotton has recently been determined by an instrument called the Micronaire. This entails the preparation of a bundle of cotton fibers of a given density through which air is passed, the air permeability being determined. All other things being equal, the flow of air is a function of the fineness of the fiber or its screening ability. Schwarz (74) discusses the measurement of fiber fineness in great detail.

**Density.** The density of fibers may be determined by classical physical means, for example, precise microscopic measurement of length and cross-sectional area, and weight. Kaswell (41), Sieminski (75), and the British Textile Institute (9) list specific gravities of the common fibers.

**Weight per Length.** The relationships among fiber length, diameter, and density result in a common and useful criterion of fiber (or yarn) size. Both weight-per-length and length-per-weight systems are utilized. The weight per length (or the inverse) of such natural fibers as wool, cotton, and flax, is not commonly measured, since staple length and diameter are usually considered sufficient to define fineness. For silk or synthetic filaments, the term denier is employed; the denier is the weight in grams of 9000 m. of filament (or yarn). The denier system is direct, that is, the "heavier" the filament or yarn, the greater is the denier.

For natural fiber *yarns* such as wool and cotton, a length-per-weight yarn numbering system is commonly used. Thus, if 840 yd. of cotton yarn weighs 1 lb., it is called a one-hank yarn or a 1s (ones). If 1,680 yd. weighs 1 lb. it is a 2s. To add to the confusion, a 1s woolen yarn (uncombed wool) contains 1,600 yd. per lb. and is called a "one run"; a 1s worsted yarn (combed wool) contains 560 yd.; and a 1s linen yarn contains 300 yd. and is called a lea.

**Cross-Sectional Shape.** Fibers vary in their cross-sectional shape (1); see also Vol. 6, p. 455. Cross-sectional shape is of prime influence in governing the stiffness and flexural rigidity characteristics of the fiber. Smith (76) discusses this relationship in detail. It has been stated that cross-sectional shape also influences the tendency of fibers to pack together in yarns. Because of their triangular shape, silk fibers can pack compactly to give small-diameter, dense yarns. Where "lofty" yarns of minimum packing are desired, irregular-shaped fibers are often suggested. However, the

position of fibers in spun yarns is normally so random that, to a large extent, yarn density becomes independent of fiber cross-sectional shape. Furthermore, in preparing lofty yarns from either staple or continuous filaments, fiber crimp (slack) is desirable in order to maintain fiber separation. The crimp effect far outweighs the effect of cross-sectional shape.

**Refractive Index.** Most textile fibers exhibit greater molecular orientation or order in their longitudinal direction than in their transverse axis. Refractive indexes are correlative with fiber orientation, and, therefore, most textile fibers have different indexes in the longitudinal and transverse directions. The quantitative difference between the two indexes is called birefringence and is a measure of the degree of the anisotropy of the fiber. Birefringence to a considerable degree directly correlates with the tensile strength properties of fibers. Refractive indexes are measurable by classical optical methods described by Preston (62,65) and Bunn (14), who also report fiber data.

**Tensile Strength.** Tensile strength is an important, but probably overworked, criterion of textile performance. Textile fibers exhibit visco-elastic behavior; that is, they do not obey Hooke's law, which states that strain is linearly proportional to applied stress. It is true that some fibers have Hookean regions in their stress-strain diagrams, but normally these are small (but not necessarily infinitesimal) portions of the graph. Because of this visco-elasticity, fiber deformations and recoveries are time-dependent. The fiber is said to exhibit "creep" upon load application, and "creep recovery" upon load removal. These do not necessarily occur at the same rate (42).

As a basis of comparison, tensile strength per weight-per-length (that is, denier) is employed. This value is called tenacity and is normally reported as grams per denier (g.p.d.). Strength may also be reported in terms more familiar to engineers, such as pounds per square inch.

Tenacity may be measured on either single filaments or parallelized fiber bundles. The usual practice with continuous filaments is to test that group of filaments which makes up what is called a producer's yarn. This may be composed of approximately 5-40 filaments twisted sufficiently to hold together as a compact yarn.

It is an extremely lengthy and laborious task to determine strength and tenacity of staple fiber, particularly cotton, because of the difficulty of manipulating single fibers, and because of the large number of tests required to obtain a significant average value. Therefore, parallel fiber bundles are tested and results reported on a pounds-per-square-inch basis. Schwarz (74) describes the Chandler and the Pressley fiber bundle tests. These normally show a lower mean strength than that for single fibers, but they are useful for mill control testing at considerably less time and expense.

The measurement of fiber strengths requires precise load-recording instruments, since the breaking load may be as low as 1 g. The development of precise electronic tension-recording instruments has been of the utmost help in fiber research activity (74). In carrying out tensile tests, single fibers are normally gripped between flat jaws, while capstan or drum-type jaws are used for yarns, in order to prevent jaw breaks. Smith (76), Kaswell (41), and Susich and Backer (78) catalog fiber tenacities.

**Elongation to Rupture.** One of the most important attributes of textile fibers is their ability to elongate under an applied load. Without this ability, they would be so completely brittle that they would be harsh, coarse, and useless. Elongations to rupture are usually measured in conjunction with the determination of tensile strength and tenacity. Smith (76), Susich and Backer (78), and Kaswell (41) list elongation values of dry and wet fibers.

**Load-Elongation Behavior.** Kaswell (41) shows load-elongation diagrams for most textile fibers. The load-elongation behavior of natural fibers is well defined. For example, wool has low strength and high elongation, whereas cotton has a significantly higher strength but appreciably less elongation to rupture. It is generally axiomatic that strength and elongation are inversely related; that is, the higher the strength, the lower the elongation. Flax is at one end of the scale, being strong and brittle (low elongation), and wool is at the other end, being highly extensible and weak. By chemical and physical means certain fiber property modifications may be made either to increase or decrease elongation, with concomitant inverse decrease or increase in strength. For example, by means of chemical swelling techniques, fiber elongation can be increased, but usually with an accompanying decrease in the tensile strength. Mercerization (see p. 875) with caustic may produce this effect on cotton or linen unless tension during treatment is rigorously controlled.

In synthetic fibers, which are made by melt-, wet- or dry-extrusion processes, the fiber is usually drawn or attenuated to improve its molecular orientation and to produce a higher tensile strength. Again, an inverse relationship between strength and elongation exists. Viscose rayon can be manufactured with low tenacity and high elongation, or with high tenacity and low elongation. By proper chemical engineering and physical control, a wide range of strength and elongation properties can be attained in almost all the synthetic fibers. As a further example, nylon can be made with a tenacity as low as 4 g.p.d. with an elongation of 40%, or a tenacity of 7½ g.p.d. with an elongation of about 12%.

**Energy Absorption.** Since the load is a force and the elongation a distance, the area under the load-elongation diagram is the product of force and distance, or work, and thus is a measure of a fiber's ability to absorb energy. Some investigators use the term toughness to describe this energy absorption (76). Coplan (20) and Kaswell (41) report on the energy absorption of fibers. Kaswell shows that equal energy absorptions may be attained with a strong, low-elongation fiber or a weak, high-elongation fiber, the areas under the load-elongation diagrams in both cases being equal. The utilization of energy and its importance as a textile parameter is shown in such applications as parachute suspension lines and tow ropes, where the kinetic energy of a moving body is converted into potential strain energy via deformation of the textile filaments. However, in addition to its significance in such applications, it is equally important wherever the textile structure is called upon to withstand repeated loads or strains at below-rupture levels. Thus, it influences abrasion resistance, flex life, crease retention, wrinkle and dimensional stability of fabrics.

**Tensional Elastic Modulus.** Young's tensional modulus is a common and valuable engineering parameter, defined as the ratio of stress (load) to strain (elongation) at loads below the elastic limit. Similar moduli exist for compression, bending, and torsion. In some engineering materials, such as steel, certain quantitative relationships exist among these four values.

Since the load-elongation diagram for most textile fibers and other high polymers is nonlinear, the ratio of load to elongation, that is, Young's modulus, is not a constant. In describing a fiber's tensional modulus, the particular portion of the load-elongation diagram selected for the calculation must be clearly defined if the resulting value is to have any significance. The ratio of rupture load to rupture elongation is sometimes calculated as an average modulus for the entire diagram.

Tensional modulus, being a measure of a fiber's resistance to deformation, is one of several factors that influence dimensional stability, abrasion resistance, and wrinkle resistance. It may also be considered a measure of fiber stiffness. However, fiber stiffness need not reflect fabric stiffness. For example, the presence of fiber crimp as it lies in the yarn, or of yarn crimp as it lies in the fabric, may contribute to a reduction in modulus of the textile structure. Meredith (50,51) and Cassie (16) list modulus values for fibers.

**Tensional Repeated Stress Properties.** Textiles normally are called upon to withstand repeated loads below rupture. The ability of a fiber to deform under such below-rupture loads and to return to its original configuration or dimension upon load removal is an important performance criterion. Thus, the repeated stress or strain characteristics become of the utmost significance in predicting or evaluating functional properties.

Hamburger (30) defines a *perfectly elastic* material as one that obeys Hooke's law, that is, the stress-strain diagram is linear and the unloading curve superimposes the loading curve. He defines a *completely elastic* material as one whose stress-strain diagram is nonlinear, whose recovery curve does not necessarily superimpose its loading curve, but whose recovery (restoration to original dimension) is complete. An *imperfectly elastic* material is one whose stress-strain diagram is nonlinear, whose recovery curve does not superimpose its loading curve, and whose recovery is incomplete.

When a fiber is stressed, the instantaneous elongation which occurs is defined as *instantaneous elastic deflection*. The subsequent delayed additional elongation which occurs with increasing time is defined as creep deflection. Upon stress removal, the instantaneous recovery which occurs is called instantaneous elastic recovery and is approximately equal to the instantaneous elastic deflection. If the subsequent creep recovery is 100% (that is, equal to the creep deflection), the specimen is said to exhibit primary creep only and is thus *completely elastic*. In such an instance, the specimen has probably not been extended beyond its yield point.

If after loading and load removal the specimen fails to recover to its original length, the portion of the creep deflection that is recoverable is still called "primary creep"; the portion that is nonrecoverable is called "secondary creep" (32). Engineers normally call this nonrecoverable elongation "permanent set."

Summarizing:

Perfect elasticity: total deflection = instantaneous elastic deflection.

Complete elasticity: total deflection = instantaneous elastic deflection plus primary creep.

Imperfect elasticity: total deflection = instantaneous elastic deflection plus primary creep plus secondary creep.

The secondary creep component of the load-elongation diagram has been given considerable attention since about 1945. It is generally accepted that, all other things being equal, the lower the secondary creep, the better is the fiber in terms of wear, shape retention, and crease resistance. This does not mean that glass, which has no secondary creep, is better in abrasion resistance than high-tenacity viscose rayon, which has secondary creep, for their respective energy absorption capacities, exclusive of secondary creep, are not equal. Nor does it mean that fibers that contain secondary creep are of no value. For the requirements of wear and crease resistance and shape retention, care must be taken that the load and extension yield points of such fibers are



not exceeded in use. For certain end-use and (particularly) processing requirements, secondary creep may be necessary in order that the fiber be permanently deformed to fit a given state of aggregation in the textile structure. For most end-uses, however, even if a flow region in the stress-strain diagram is required, it is advantageous to obtain this flow region by primary rather than secondary creep.

Hamburger (30) also employs the term elastic performance coefficient (E.P.C.) as a criterion of repeated stress performance. This value reflects the effect of immediate elastic, primary, and secondary creep deflections, and, in addition, the ability of the material repeatedly to absorb and return energy during repeated stressing. The importance of energy-absorbing ability is evident, since to resist destruction the specimen must be capable of absorbing energy imparted to it upon stress application, and of releasing this energy upon stress removal without failure. The E.P.C. is a normalized index that expresses degree of perfect elasticity. A material that exhibits identical elastic properties after repeated stressing with those which it had originally (in one-time loading) has an E.P.C. of 1.0. Similarly, a perfectly viscous material with no recovery has an E.P.C. of zero.

**Fiber Deformations Other than Tensional.** Textiles are called upon to withstand deformations other than tensile, and the bending and torsion properties of fibers may become equally important relative to textile performance. Referring to classical, physical concepts, there are five simple types of elastic deformation (41): simple tension, compression, shear, torsion, and bending.

In order to be useful, textile fibers must be flexible. Smith (76) shows that the stiffness of an ideal cylindrical rod is proportional to the square of the denier. Since the denier, in turn, is proportional to the square of the diameter, it is seen that stiffness increases as the fourth power of the filament diameter. The shape of the filament cross section also must be considered, as is demonstrated by the fact that I-beams are so made because they exhibit high rigidity per unit weight. Finlayson (22), reports on the filament deniers required to give equal filament flexibility.

*Bending Fatigue and Shear.* Thomson and Traill (80) discuss the resistance of fibers to repetitive bending. Finlayson (23) reports on the shear properties of fibers. The problem of shear usually is of much greater significance in brittle high-modulus materials, where, although absolute shear strengths are higher than for low-modulus materials, inability to deform causes the development of extremely high stress concentrations at certain points (for example, at the crossover of a warp and filling yarn), and failure results. This is a disadvantage of glass. For textile purposes, where flexibility is a requisite, Platt (59) demonstrates that shear bending and torsional stresses are relatively minor factors when compared with tensional stresses.

*Loop Strength and Knot Strength* (see Vol. 11, p. 548). Coplan (20) reports on the loop strength of textile fibers. Kaswell (41) shows a general trend indicating a direct relationship between tensile elongation to rupture and loop strength efficiency. Millard (45) and Schiefer, Fourt, and Kropf (71) report on knot strength values.

**Friction.** Fabric properties that are governed in part by frictional effects are fabric hand, strength, elongation, abrasion resistance, dimensional stability, and seam slippage. The conversion of staple fibers into yarns is dependent upon friction, as are many of the subsequent manufacturing operations, particularly procedures employed in wet-finishing of wool. Particular emphasis is given in the literature to wool and animal hair, since they are probably the only fibers that exhibit two frictional effects, depending upon whether the relative motion is with or against their scales.

Fiber friction can be determined by physical methods. Fuller and Johnson define and derive the calculation of friction coefficient. Speakman and Stott (77) measure fiber friction by a violin bow technique. A series of parallel fibers are clamped across a small bridge, and the coefficient of friction across the series of fibers is determined in the usual fashion against any selected material. Several investigators (13,47,54) use the well-known belt friction formula, wherein a belt of yarn or fiber slips over a cylindrical surface. The tension  $t_1$  and  $t_2$  at two ends of the belt and the angle of contact  $\theta$  being known, the friction coefficient  $\mu$  can be determined according to the formula:

$$t_1/t_2 = e^{\mu\theta}$$

Lindberg and Gralen (44) use the force required to pull two entwined fibers apart and thus measure friction coefficient. Mercer and Makinson (49) and Bowden and Leben (7) use an apparatus wherein a fiber is mounted on a glass bow and is pressed against a surface that may be another fiber or some other surface. The technique is called a slip-stick method because the fibers alternately slip and stick as they slide across each other. Mercer and Makinson (49) and Lindberg and Gralen (44) show that friction coefficient is not constant with normal pressure but varies with load in hyperbolic fashion.

**Moisture Absorption.** *Moisture regain* is defined as the loss in weight of water upon drying, as a function of the dry fiber weight. *Moisture content* is defined as the same weight loss, as a function of the combined fiber and water weight. The normal method of determining these values consists in weighing, bone-drying, weighing, and calculating. Carlene (15) lists moisture regain values at standard testing conditions of 65% r.h. and 70°F. Fibers that are capable of absorbing water, when exposed to progressively increasing and then decreasing relative humidities, show regain versus relative humidity curves which do not coincide. The area between the two curves (amount of hysteresis) is generally directly correlative with the moisture regain determined at standard conditions.

Since the mechanical properties of the hydrophilic fibers are critically dependent upon moisture regain, it is vital that such materials be tested under constant conditions of temperature and humidity. The textile industry has selected 65% r.h. and 70°F. as standard for all testing (1,3,9,81).

**Heat of Water Absorption.** When textile fibers absorb water, they evolve heat. Heat of absorption is defined as the heat evolved when 1 g. of water is absorbed in a large mass of fiber (52). Meredith (52) shows that the heat of wetting of a fiber is linearly related to its moisture regain. Thus, when moisture regain at 65% r.h. and 70°F. is plotted versus the heat evolved in bringing the fiber from the bone-dry condition to equilibrium at 65% r.h., a straight line results for nylon, cotton, silk, viscose rayon, and wool (41,52).

**Fiber Swelling.** When fibers absorb water, they swell both radially and longitudinally. As a general qualitative rule it can be stated that, the greater the ability of the fiber to swell, the greater is the moisture regain. The amount of moisture regain and swelling is a function of the ability of the fiber to absorb water and is dependent upon the amorphous regions of the fibers, Meredith (52) stating that little water enters the crystalline regions. Meredith (52), Preston (62, p. 40), and Preston and Nimkar (66) give considerable information on the swelling mechanics and properties of fibers.

*Effect of Moisture on Mechanical Properties of Fibers.* Since textiles, in processing, are sized, bleached, dyed, and finished, they must have requisite characteristics in tension, torsion, and bending to withstand the required wet-finishing operations. For example, the yield point must not be reduced by wetting to a value such that the resulting wet fiber or fabric cannot be processed without becoming permanently and irrevocably distorted. Wetting the fabric, however, is necessary in many finishing operations. The ability of a fiber to be rendered plastic by water, whereupon it can be "molded" into a required geometric configuration and then "set" in that configuration by redrying, is the basis of many finishing operations. Similarly, if the fiber is to be used in any environment where it is apt to become wet or subjected to high humidities, it must be able to withstand such conditions.

As might be expected, there is little difference between the wet and dry stress-strain diagrams of the hydrophobic fibers—nylon, Orlon, Dacron, etc. The hydrophilic protein fibers and regenerated celluloses exhibit lower tensional moduli on wetting out, that is, their elongations increase while their strengths diminish. The hydrophilic natural cellulosic fibers, cotton, linen, and ramie, are stronger wet than dry. Hindman and Fox (37), Coplan (20), and Meredith (52) show the effect of moisture vapor and water on the load-elongation diagram.

**Thermal Conductivity.** Most fibers have thermal conductivities of the same order of magnitude. It is generally agreed that the thermal-insulation ability of a fabric is dependent upon the state of aggregation of fibers in yarn, and yarns in fabric, rather than upon intrinsic fiber conductivity. Cassie (16) states that the heat insulation of a fabric results from the air entrapped in it. Baxter (6) has determined fiber conductivity by determining for various bats (fiber aggregates) of materials, a curve of thermal conductivity versus bat density. The curve is extrapolated to determine conductivity at a bat density equal to fiber density.

**Heat Capacity.** Dietz (21) shows that most fibers have heat capacities of the same order of magnitude. Thus, this parameter has but a negligible effect on the thermal insulation properties of textile structures.

**Thermal Stability.** Textile fibers may be classified into two main groups with respect to their reaction to heat: thermoplastic and nonthermoplastic. Most synthetic fibers, with the exception of the regenerated proteins or celluloses, are thermoplastic, whereas the natural fibers, wool, cotton, linen, and silk, are nonthermoplastic.

Fiber degradation due to heat is affected by temperature, time of exposure, relative humidity, and air circulation. Air circulation may be important because many aging or heat-degradation processes involve oxidation, and, the greater the air circulation, the more oxygen there is available to the fiber. With respect to ironing and pressing, pressure and heat transfer also affect the amount of degradation. Newell (55), Ray (67), and Brown (10) all list the effect of heat on fibers. Preston (64) lists both contraction temperatures and melting points of thermoplastic fibers. It should be pointed out, however, that most thermoplastic fibers have no precise melting point in the sense that the organic chemist applies such a term to the property of an organic chemical compound. The fiber has a temperature-sensitive range, while the polymer from which the fiber is made may or may not have a clearly measurable melting point.

**Flammability of Fibers.** See Vol. 6, p. 544. Flame burning tests may be used as a means of identifying fibers. The British Textile Institute (9) lists a complete series of flame tests for aid in the identification of textile fibers. These tests differ from determinations of flammability. See Vol. 6, p. 556.

**Stability of Fibers to Environmental Conditions.** *Modern Plastics Encyclopedia* (53) lists the effects of aging, sunlight, and prolonged weathering on textile fibers. Fletcher (24) notes the effects of heat and light on the properties of curtain fabrics. *Modern Plastics Encyclopedia* (53) and Newell (55) list general chemical resistance of fibers. *Fibre Science* (63) gives a comprehensive treatise on the chemical reactivity of most of the natural and synthetic fibers. The criterion usually employed to measure degradation is breaking strength. However, other criteria are also used, depending upon the performance requirements.

**Electrostatic Properties.** Static electricity is normally generated when two different materials are rubbed together. If the resulting charges are retained and accumulated, a potential is generated that becomes apparent (43). If the material under consideration is a conductor and is grounded, the charge will be removed as fast as it is deposited, and no static electricity is observed. However, if the material is a dielectric, charge will build up to the point where it may interfere with textile processing (inability to card, spin, etc.) or be objectionable to a person wearing the material because of its clinging, sparking, and the like.

At present (1954) the subject of static electricity measurement is under intensive study, but there are no standard acceptable test instruments or methods of measurement. Four criteria are currently being employed: (1) surface resistivity; (2) volume resistivity; (3) rate of charge build-up and leak-off; (4) maximum charge capable of being retained.

The synthetic hydrophobic fibers have high dielectric strengths and thus are excellent electrostatic generators. The natural and synthetic hydrophilic fibers, because of their higher moisture regains, present less of a processing and use problem, particularly at high relative humidities. However, at low relative humidities these fibers also present electrostatic problems. Lehmicke (43) points out that, although electrostatic properties are influenced by intrinsic fiber properties and moisture regain, these two parameters do not completely explain the electrostatic ranking of the various fibers.

### Yarn and Fabric Geometry Effects

Because of the complexity of fabric geometry studies, the subject has been investigated to a much lesser extent than have inherent fiber properties. Two approaches to the problem have been made: (1) theoretical analyses of ideal geometric structures, and (2) empirical investigations of the effects of geometry on physical properties. See references 4,5,56,58,60,61,72. Those geometric factors that relate inherent fiber properties to fabric properties are discussed below. Obviously, the relationship between inherent property and geometric form must never be neglected.

Many inherent and geometric form properties are measurable in quantitative terms on the basis of scientific knowledge, independently of personal preferences or reactions; that is, they are *objective*.

There are certain equally important *subjective* performance characteristics that are evaluated at least in part by personal reaction. These can be expressed in qualitative terms, although quantitative physical parameters in part govern the subjective measurements. Fabric hand (or handle), drape, color, and luster are at least in part in this category.

### OBJECTIVE TESTS

**Compressional Resilience.** The textile industry uses many words in a qualitative sense which are often difficult, if not impossible, to define precisely. The word re-

resilience is not always used to mean complete and instantaneous recovery after deformation, although textile physicists are currently attempting to give it this precise meaning (30,65). The A.S.T.M. (2) lists a series of terms that relate to the hand of fabrics; the influence of compressional resilience is included. The importance of compressional resilience and other deformation-recovery characteristics of textile fabrics may be noted in such end-use requirements as wrinkle resistance, retention of shape, drape, and hand, including softness, stiffness, harshness, limpness, liveliness, boardiness, and springiness, all of which are dependent upon the resilience of the structure. Resilience is an important parameter for evaluating blankets and wearing apparel in which warmth is a factor; permanency of pile fabrics including carpets; and bulk fiber utilization in mattresses, cushions, and the like.

With respect to comfort in clothing, warmth is dependent upon thermal conductivity, air permeability, and moisture transmission. Thermal conductivity is inversely related to fabric thickness, and maintenance of thickness is vital to the maintenance of warmth. Since compressional resilience reflects the ability of a fabric to maintain its original thickness, it may be used as one of the criteria of warmth.

The general method for determining compressional resilience is to compress and unload the material cyclically and then plot a repeated stress diagram (compressive force versus thickness of fabric). Hamburger (30), uses elastic performance coefficient (see p. 913) to measure compressional resilience.

Kaswell (41) shows that bulk compressional resilience is directly related to the tensional elastic recovery properties of fibers. Since in compressing bulk fibers they are subjected to tensional strains resulting from bending and other types of deformations, one would expect that compressional resilience would be related to tensional elastic recovery properties. On the other hand, bulk compressibility, that is, the ability of bulk fiber aggregates to be compressed, is independent of tensional elasticity.

**Thermal Transmission.** True thermal conductivity or insulating ability must be distinguished from the subjective feeling of warmth (or coolness) by a human subject. The former is defined in strict engineering terms and is one of the factors involved in warmth. The latter is a physiological and psychological measure definable in terms of body comfort. It has been reasonably well established that warmth or coolness is a sensation produced by the interaction of several factors: thermal conductivity, convection, radiation, moisture transfer, air transfer, fabric texture, fabric smoothness, and roughness.

Since the thermal conductivity of air is lower than that of fibers, it follows that, the greater the entrapment of dead air space within a textile structure, the better is the insulating ability. Marsh (46) shows an almost linear relationship between thermal insulating value and fabric thickness and states that the chief (but not the sole) factor that determines the thermal insulation value is thickness. He finds almost no correlation between thermal insulation and weight per unit area.

*Thermal Transmission vs. Fabric Density.* Considering that fiber conductivity has little effect upon a fabric's thermal transmission, as well as the conductivity-thickness relationship, it becomes obvious that state of aggregation of the fiber in the fabric structure is of major importance. As long as the required thickness is maintained, concomitant insulation will result. However, the ability to maintain thickness under normal use conditions of compression, tension, bending, laundering, dry cleaning, and wear must not be overlooked.

One additional factor which must be discussed is fabric density. Two fabrics

may have the same thickness, and hence the same thermal conductivity, but, to obtain such equal thicknesses, different weights of fiber may be needed. Thus, aggregates of different fibers may have different bulk densities, and on this weight basis one fiber may exhibit thermal insulating advantage over another.

*Effect of Air Velocity on Thermal Transmission.* Rees (68) shows that fabric structure rather than fiber properties governs fabric air velocity. Platt and Chu show that air moves within the interstices of yarn and fabric rather than within the fiber. Thus, air permeability is influenced by the void spaces within the textile structure. Since the same void space is influential in controlling thermal conductivity, it follows that thermal conductivity is influenced by air permeability. However, the movement of air through a textile structure can dissipate heat by convection because the air is no longer "dead air." Thus, the thermal insulation will fall as the air velocity rises. Rees (68) also shows that relative humidity has a negligible effect upon heat transmission.

**Air Permeability.** Air permeability plays an important part in certain limited end-use requirements such as parachute fabrics, boat sails, clothing in which warmth is desired, rainwear and other water-impermeable fabrics, and industrial air filters. It is normally measured as the volume of air per unit time flowing through a given area of the fabric at a selected pressure differential across the fabric, usually one-half inch of water. Platt and Chu show that air flow through a fabric may be calculated with reasonable accuracy by classical fluid mechanics procedures. By means of Bernoulli's energy equation and the equation of continuity, air flow has been shown to be proportional to the square root of the pressure differential. A discharge coefficient is a characteristic of the orifices, but the discharge coefficient normally used in fluid mechanics calculations must be modified to include the effects of the geometrical changes in the fabric resulting from the application of air pressure.

**Moisture Transmission.** Water vapor permeability is an important parameter concerned with the suitability of fabrics for apparel purposes.

Fourt and Harris (25) suggest two methods for measuring the diffusion of moisture through a fabric barrier: the absorption cup method and the evaporation method. The former consists in ascertaining the amount of water which will diffuse through the test fabric and into a cup of drying agent, the test fabric acting as the cover of the vessel containing the desiccant. The other side of the fabric is exposed to an atmosphere of constant humidity, temperature, and air velocity. The amount of water absorbed per unit area per unit time can be calculated by determining the increase in weight of the desiccant at selected time intervals. The evaporation method consists in placing the test fabric over a carefully calibrated cup filled with water to a prescribed depth. Again, the cup and fabric assembly is exposed to an atmosphere of constant humidity, temperature, and air velocity, and the rate of loss in weight of water in the cup is determined.

If it is assumed that a moisture differential exists between two sides of a fabric, water vapor may pass either through the fabric interstices or through the fibers themselves. The contribution of each may vary from 0 to 100%. If, in a hydrophilic fiber fabric the weave is open, moisture will pass through the fabric's interstices and through the fiber *per se*. If the weave is extremely tight, moisture will pass primarily through the fibers. Body comfort in both cases is about equal, probably because sufficient moisture can pass via either path. Thus hydrophilic fibers are comfortable in so far as moisture transfer is concerned under all conditions of fabric structure.

With hydrophobic fibers, if the weave is open, moisture will transfer through the fabric interstices, and the wearer will be comfortable. If the weave is tight, moisture cannot transfer either through the fabric interstices or through the fibers *per se*, and a wearer may be uncomfortable because of the lack of moisture dissipation. Thus hydrophobic fibers should be used with care to assure that fabric construction permits moisture transfer.

**Water Repellency and Water Resistance** (see *Waterproofing*). The A.A.T.C.C. *Yearbook* (1) states that *water repellency* is the ability of a textile fiber, yarn, or fabric to resist wetting. *Water resistance* is a general term denoting the ability of a fabric to resist wetting and penetration by water. The American Society for Testing Materials uses similar definitions for water repellency and almost identical definitions for water resistance. The A.A.T.C.C. *Yearbook* (1) lists the following test methods for measuring water repellency and water resistance: resistance to hydrostatic pressure; resistance to absorption of water during immersion; resistance to penetration of water by impact; resistance to water spray; resistance to rain test.

Rowen and Gagliardi (69) use the terms "waterproof" and "water-repellent." A waterproof fabric is defined as one in which the pores or interstices between fibers and between yarns are filled with appropriate substances which cause the fabric to have a continuous surface and very small air permeability. A water-repellent fabric is (69) "one whose fibers are usually coated with a hydrophobic type compound and whose pores are not filled in the course of the treatment. The latter types of fabrics are quite permeable to air and water vapor."

Basic methods for measuring water repellency or water resistance are: (a) measurement of pressure required to force water through a fabric; (b) measurement of amount of surface wetting or penetration via falling droplets; (c) measurement of water absorption upon immersion; (d) measurement of fiber or fabric wettability via contact angle. Kaswell (41) gives a detailed description and summation of all test methods.

The hydrophilic fibers can absorb and transfer water, and as such they are not naturally water-repellent. They can be utilized for wet weather textiles only if external water-repellent finishes are applied. The hydrophobic fibers do not need water repellency treatments *per se*, but the fabrics into which they are made may be of a construction such that a water-repellent treatment might still be needed to prevent the water's rolling or wicking through the interstices of the yarns and fabric.

With hydrophobic fibers, fabric structure to a large degree will control water repellency. The factor that most synthetic fibers can pack closely is conducive to making tight fabrics from them. However, if the fabric is sufficiently tight to repel water by high "jamming" of yarns, the problems of moisture vapor transfer and body comfort appear. If it is assumed that a compromise can be made between tightness of structure and body comfort by means of chemical water-repellency treatments, it would be expected that fabrics made from inherently water-impermeable synthetic fibers should provide excellent water repellency.

A review of the methods whereby fibers can be formed into water-repellent fabrics shows that there are three distinct mechanisms for attaining such fabrics:

(1) Close packed structures composed of either hydrophobic or hydrophilic yarns with chemical water-repellent finishes as they might be needed. This group is the most popular and includes water-repellent treated cotton fabrics.

(2) Relatively open hydrophilic wool or fur constructions, wherein the fibers are

uniformly spaced and held as far apart as possible so that water droplets which strike become absorbed with difficulty.

(3) Soft cotton yarn constructions such that the initial portion of water striking the fabric swells the fibers and thereby closes the interstices.

**Crease Retention and Wrinkle Resistance.** On bending or creasing a textile material, the external portion of each filament is placed in tension while the internal portion is placed in compression. Thus, the wrinkle recovery properties must be governed in part by the inherent, tensional elastic deformation and recovery properties of the fibers going to make up the yarns and fabrics. In addition to the inherent fiber properties, the yarn and fabric states of aggregation, that is, yarn and fabric geometry, must also be taken into consideration (26,32).

Buck and McCord (11) and Kaswell (41) give complete descriptions of various laboratory test methods for measuring wrinkle resistance and crease retention. These range from qualitative random wrinkling by a "clenched fist" squeeze and relaxation to quantitative measurement of recovery angle after a specimen is creased in a prescribed reproducible manner. The most popular of the latter methods is the Tootal-Broadhurst-Lee (T.B.L.) test. This consists in folding a sample 4 x 1 cm. in the middle under a prescribed pressure for a given length of time and then allowing it to recover while hanging over a pin. The recovery angle is then measured as a criterion of wrinkle resistance. The basic T.B.L. method has been mechanized in more elaborate fashion, employing an apparatus designed by Monsanto Chemical Co. called the Monsanto Wrinkle Recovery Tester, as well as one by American Cyanamid Co. called the Roller Pressure Tester. Recently the Stoll-Celanese wrinkle tester has been marketed and is now being studied.

Because of the relative simplicity of the Monsanto tester, it has had fairly wide adoption as a standard test instrument. Generally speaking, those materials which exhibit Monsanto recovery angles greater than  $115^\circ$  are considered to exhibit good wrinkle-resistance performance under service conditions. This does not mean that every fabric which tests over  $115^\circ$  automatically will give proper wrinkle-resistance performance in service. Since wrinkle resistance is particularly important for summer clothing, the A.A.T.C.C. stipulates that crease recovery angles be measured at a relative humidity of 90%, as well as at the standard 65% r.h. The 90% r.h. is considered to represent the most humid condition to which apparel textiles may be subjected in summer.

Buck and McCord (11) discuss the effects on wrinkle resistance of fiber staple length, diameter, and shape, of yarn construction, twist, and diameter, and of fabric weave, weight, and thickness.

**Abrasion and Wear Resistance.** Most textile technologists confine the term abrasion to a simple rubbing action as might occur with a laboratory abrasion tester. The term wear is broader in scope and includes the combined effect of many additional factors beside abrasion, for example, laundering, dry cleaning, ironing, and wearing of apparel.

Prediction of general wear resistance from a laboratory abrasion test is hazardous, and the relationship between laboratory abrasion tests and service performance has been the subject of intensive study. The five laboratory abrasion testers most commonly used in the U.S. are the Taber, United States Testing Co., Wyzenbeek, Schiefer, and Stoll abraders. Methods for the determination of abrasion resistance using these testers are described in A.S.T.M. Designation D 51T (3).

With respect to the relationship between inherent fiber properties and abrasion



resistance, Vogt (82) suggests a possible relationship between energy absorption and abrasion resistance in rubber. Hamburger (29) states that abrasion is a series of repeated stress applications, usually caused by forces of a relatively low order of magnitude, which occur many times during the life expectancy of the material. Hence the ability of a material to absorb energy repeatedly by means of low load deformation and recovery is related to abrasion resistance. All deformation components of the stress strain diagram (see p. 911), namely, instantaneous elastic deflection, primary creep, and secondary creep, contribute to total energy absorption.

However, secondary creep may be removed by means of a relatively few loading and unloading cycles. For a material to resist abrasion, it must withstand many cycles. While secondary creep is an energy-absorbing component of an "original" load-elongation diagram to rupture, its contribution under repeated loading below rupture is negligible since it is removed in the course of the first few cycles. Thus it contributes little to abrasion resistance. Both immediate elastic deflection and primary creep deflection are recoverable upon load removal. They contribute to both the absorption and return of energy necessary for proper performance under repeated stress and as such influence abrasion resistance.

Hamburger lists five requirements for high abrasion resistance: low modulus of elasticity, large immediate elastic deflection, high ratio of primary to secondary creep, high magnitude of primary creep, and high rate of creep recovery.

Backer (4) discusses abrasion mechanisms by analyzing the effects of an abrasive particle upon a fiber surface. He states that a fiber can be abraded:

(1) By frictional wear such as occurs when smooth metal surfaces are rubbed together; for example, the surface-polishing of furniture.

(2) Where surface projections of the abrading surface are small relative to fiber diameter, the fiber will be subjected to a surface-cutting process such as occurs in metal cutting or grinding. Such wear will occur when a very fine abrasive or emery surface is rubbed across the fabric.

(3) Where the surface protuberances of the abradant are large compared to fiber diameter, and the normal forces between the abradant and the cloth planes are high, the fiber will then be plucked.

The three mechanisms are thus frictional wear, surface cutting, and fiber rupture or slippage.

Fabric geometry is of great significance with respect to the abrasion resistance of fabrics. Kaswell (40) analyzes the effect of weave on abrasion resistance, as well as the relationship between abrasion resistance as measured in the laboratory and service performance. Backer and Tannenhaus (5) discuss the following factors which affect abrasion resistance: geometric area of contact between fabric and abradant; local pressures or stress concentrations which develop on specific yarn points or areas; threads per inch; crown height, that is, the extent of deformation out of the plane of the fabric resulting from the intersection of warp and filling yarns; yarn size; fabric thickness; yarn crimp; float length; yarn cohesiveness; compressive compliance, that is, compressional resilience of the fabric and backing; fabric tightness; cover factor; direction of abrasion; and magnitude and direction of tensions developed during abrasive action.

**Laundering Shrinkage.** When textile fabrics are wet-laundered, they often shrink. Shrinkage is of two types: relaxation and felting. The former (28) takes place when a fabric (usually composed of hydrophilic fibers) is wet out. Felting shrinkage is

associated exclusively with wool and other animal fibers which are feltable in the practical sense. It entails the continued reduction in fabric area and the continued increase in fabric density due to the application of heat, moisture, and mechanical motion occasioned by the water washing.

Fabric relaxation shrinkage is not the result of linear fiber shrinkage because the hydrophilic (wool, silk, cotton, viscose) and partially hydrophilic fibers (nylon, cellulose acetate) all increase in length on wetting out. However, there is an appreciable increase in fiber diameter for the hydrophilic fibers which is a direct cause of fabric shrinkage. Collins (19) states that shrinkage does not occur unless water gains access to the material by one means or another. When this occurs, shrinkage takes place via swelling and release of strains. Collins shows that fiber-diameter swelling causes yarn-diameter swelling, and this in turn causes a forced increase in yarn crimp. To accommodate this increase, the threads of which the fabric is composed move closer together and shrinkage is the net effect.

Since the hydrophobic fibers do not swell, they do not shrink when wet-laundered. It should be pointed out that some hydrophobic fibers are susceptible to thermal shrinkage, and the effect of the hot water used in laundering may cause fabric shrinkage.

#### SUBJECTIVE TESTS

**Fabric "Hand" or "Handle."** Schwarz (74) defines handle as the "feel" of the material and qualitatively includes such terms as stiffness (or limpness), hardness (or softness), and roughness (or smoothness). Similarly, Hoffman and Beste (38) define hand as the impression which arises when fabrics are touched, squeezed, rubbed, or otherwise handled. See also references (3) and (76).

It will immediately be evident that, whereas the words feel and hand are subjective, the parameters which contribute in part to this subjective reaction can readily be measured quantitatively. Thus stiffness can be measured by such means as the deflection of a cantilever beam; hardness by measurement of compressional resilience; and roughness by the coefficient of friction. The last two properties have previously been considered (see pp. 914,916).

**Bending Length.** Peirce (57) measures flexibility by the determination of a cantilever "bending length" test. A specimen 6 x 1 in. is extended lengthwise over an edge, the force of gravity causing it to deflect from the horizontal. From the relationship between the deflected length and accompanying angle subtended, the "bending length" can be calculated. The stiffer the material, the greater is the bending length.

**Flexural Rigidity.** Peirce (57) further states that, while bending length is a measure of stiffness, flexural rigidity is a measure of the resistance to bending "as appreciated by the fingers." Two fabrics may bend to the same extent under their own weight, but the heavier of the two will exert more resistance to bending and so will feel stiffer. Flexural rigidity ( $G$ ) is related to bending length ( $c$ ) by the equation  $G = wc^3$ , where  $w$  is the fabric weight per area.

To define fabric hand, Peirce also lists the following parameters: thickness, hardness, bending modulus (related to flexural rigidity via thickness), compression modulus, density, and extensibility.

In addition to Peirce's criteria, certain test instruments are generally employed to measure various stiffness properties: the Gurley, the Clark, and the Olson stiffness testers, and the Schiefer Flexometer (41).

**Fabric Drape.** Whereas hand implies tactile criteria, drape is normally construed to depict a visual reaction to the fabric's appearance, for example, its tendency

to fall into pleasing and graceful folds. However, fabric drape is dependent to a large degree on the same properties that influence fabric hand, e.g., stiffness, flexural rigidity, thickness, and compressibility. However, while stiffness is normally measured in a single direction, drape implies bending in all directions and has a three-dimensional aspect to its deformation.

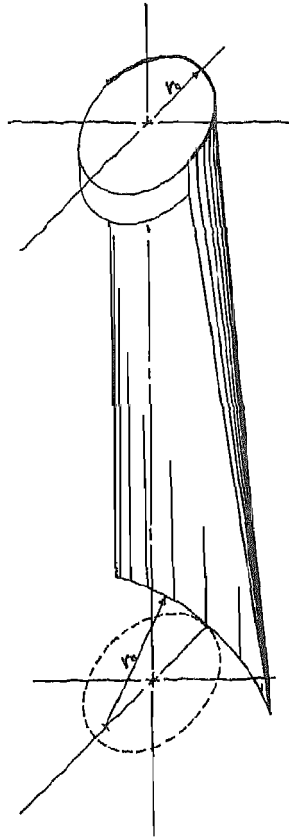


Fig. 1. Sketch of the principle of the M.I.T. Drape-o-meter (41).

Two instruments have been developed to measure fabric drape, the M.I.T. Drape-o-meter (73) and the Fabric Research Laboratories' Drapemeter (17). The M.I.T. Drape-o-meter measures the rate of change of radius of curvature which takes place when the fabric is bent about a cylinder (Figure 1). The F.R.L. Drapemeter employs a horizontal circular specimen (say) 10 in. in diameter which is placed concentrically over supporting disk (say) 5 in. in diameter. The fabric overlap is deflected downward and assumes a "draped" configuration depending upon its multi-directional stiffness and flexibility. Thus various areas of the specimen are bent in three varying directions relative to themselves. Figure 2 is a diagram of the position assumed by a fabric section. The projected area as a percentage of the theoretical maximum area is a measure of the degree of drape.

Preliminary research upon the subjects of handle and drape shows that people

are more capable of tactilely ranking fabrics for stiffness, flexural rigidity, and "hand" than they are for visually ranking them for drape (31).

**Color.** Color is an excellent example of the relationships that have been developed in recent years between subjective and objective property measurement.

Colors have been classified into organized subjective systems; representative are those suggested by Munsell, Ostwald, and the International Committee for Illumination. Classification considers hue or shade, value or degree of grayness (from black to white), and chroma or intensity of shade. See *Color (measurement)*.

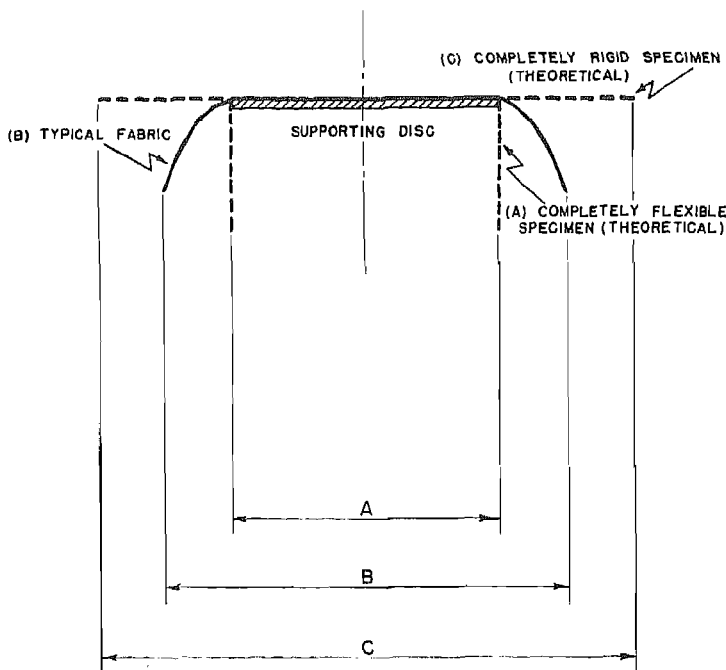


Fig. 2. Drapemeter diagram(41). A. Theoretical condition of complete flexibility wherein projected area equals supporting disk area. B. Typical fabric condition. C. Theoretical condition of complete rigidity wherein projected area equals sample area.

Quantitatively, color can be measured by means of the spectrophotometer. This instrument measures the percentage of light of a given wave length, which is reflected from, or transmitted through, a colored specimen, as a function of the total light incident upon the specimen. Plots of per cent reflectance or transmission versus wave length in the visible range (400–700  $m\mu$ ) are usually obtained in order to describe a color precisely. The same three parameters, namely, hue, value, and chroma which are utilized subjectively are also obtainable from spectrophotometric curves and are therefore used in the quantitative measurement of color. See *Colorimetry*.

**Luster.** Luster is dependent upon both inherent fiber and yarn and fabric geometry properties in so far as they control the degree of order or regularity of surface from which light can be reflected. Surface irregularities, wherever they may occur, tend to diminish the degree of luster. The greater the degree of parallelization of

fibers in yarns, and of yarns in fabrics, the greater is the amount of luster. Similarly, in fabrics, the longer the float (number of filling yarns, for example, which a perpendicular warp yarn crosses over before actually intersecting the filling yarn) and the smaller the number of warp and filling yarn intersections, the greater is the degree of luster. This is why satins are so shiny.

Buck and McCord (12) state that luster defies complete measurement in quantitative terms, there being both subjective and objective aspects to the measurement. Harrison (35) outlines six methods for measuring luster, but only three are applicable to textiles (12). These are:

(1) Determination of the amount of light which a surface can reflect specularly. Light falls on the test sample from some chosen angle, usually between  $45^\circ$  and  $80^\circ$  to the normal, and the intensity of reflected light is measured from the corresponding specular angle.

(2) The contrast between specular and diffuse reflection is measured subjectively, on the premise that such contrasts contribute most effectively to the visual impression of luster.

(3) Goniophotometric methods are the fundamental physical methods for studying the lustrous or light-reflecting properties of surfaces. The intensity of reflected light is observed at all angles in the plane containing the angle of incidence. A curve or family of curves is obtained which rather completely describe the light-reflecting properties of the material.

Buck and McCord (12) state that each of the three general methods listed above will give some interpretation of the effect of color if color filters are used. There is no assurance, however, that the instruments thus modified will be affected by color in the same manner as are the eyes. Moreover, none of the methods adequately interprets the texture and binocular effects of which the eyes are so conscious. Therefore, it seems likely that visual observations will continue to be necessary for the final appraisal of textile luster.

### Bibliography

- (1) A.A.T.C.C., *1953 Yearbook*, p. 29.
- (2) A.S.T.M. Committee D-13, "Terms Relating to Hand," Supplement III, A.S.T.M. Standard P-370, 1943.
- (3) A.S.T.M. *Yearbook on Textile Test Methods*, Committee D-13, 1954.
- (4) Backer, S., *Textile Research J.*, **21**, 453 (1951).
- (5) Backer, S., and Tannenhaus, S., *Textile Research J.*, **21**, 635 (1951).
- (6) Baxter, S., *Proc. Phys. Soc. (London)*, **58**, 105 (1946).
- (7) Bowden, F. P., and Leben, L., *Proc. Royal Soc. (London)*, **169**, 371 (1939).
- (8) *Brit. J. Appl. Phys.*, "Static Electricity," Supplement No. 2, 1953.
- (9) British Textile Institute, "Identification of Textile Materials," *J. Textile Inst.*, **42**, 825 (1951).
- (10) Brown, R., *et al.*, *Ind. Eng. Chem.*, **40**, 1773 (1948).
- (11) Buck, G., and McCord, F., *Textile Research J.*, **19**, 216 (1949).
- (12) Buck, G., and McCord, F., *Textile Research J.*, **19**, 715 (1949).
- (13) Buckle, H., and Pollitt, J., *J. Textile Inst.*, **39**, T199 (1948).
- (14) Bunn, C. C., "Optical Properties of Fibers," in *Fibre Science*, J. M. Preston, ed., British Textile Institute, Manchester, 1949.
- (15) Carlene, P. W., *J. Soc. Dyers Colourists*, **60**, 232 (1944).
- (16) Cassie, A. B. D., *J. Textile Inst.*, **37**, 556 (1946).
- (17) Chu, C., Cummings, C., and Teixeira, N., *Textile Research J.*, **20**, 539 (1950).
- (18) Church, J. M., in *Flameproofing Textile Fabrics*, R. W. Little, ed., Reinhold, N. Y., 1947.
- (19) Collins, G. E., *J. Textile Inst.*, **30**, P46 (1939).

- (20) Coplan, M. J., "The Effect of Temperature on Textile Materials." Document 53-21, Wright Air Development Centre, Dayton, Ohio.
- (21) Dietz, "Specific Heat Capacity of Fibers," in Matthews' *Textile Fibers*, 4th ed., Wiley, N.Y., 1943, p. 9.
- (22) Finlayson, D., *J. Textile Inst.*, **37**, 168 (1946).
- (23) Finlayson, D., *J. Textile Inst.*, **38**, T50 (1947).
- (24) Fletcher, H. M., *Am. Dyestuff Repr.*, **38**, 603 (1949).
- (25) Fourt, L., and Harris, M., *Textile Research J.*, **17**, 256 (1947).
- (26) Gagliardi, D., and Grunfest, I., *Textile Research J.*, **20**, 180 (1950).
- (27) Gonsalves, V., *Textile Research J.*, **23**, No. 10 (Oct. 1953).
- (28) Gould, J., *Am. Dyestuff Repr.*, **38**, 407 (1949).
- (29) Hamburger, W. J., *Textile Research J.*, **15**, 169 (1945).
- (30) Hamburger, W. J., *Textile Research J.*, **18**, 102 (1948).
- (31) Hamburger, W. J., Platt, M. M., and Chu, C., "Factors which Influence the Draping Properties of Cotton Fabrics," Fabric Research Laboratories, Inc., Report 966.
- (32) Hamburger, W. J., Platt, M. M., and Morgan H. M., *Textile Research J.*, **22**, 695 (1952).
- (33) Hamburger, W. J., Platt, M. M., and Ross, M. W., "A Study of the Effects of Form Factors on the Translation of the Inherent Physical Properties of Textile Fibers into Textile Structures," Office of the Quartermaster General, Textile Series Report No. 59, Washington, D.C.
- (34) Hardy, J., "Heat Transfer," in *Physiology of Heat Regulation and the Science of Clothing*, L. H. Newburgh, ed., Saunders, Philadelphia, 1949.
- (35) Harrison, S., *Measurement of Gloss*, Printing and Allied Trades Research Association, 1945.
- (36) Hearle, J. W. S., *J. Textile Institute*, **44**, T117 (1953).
- (37) Hindman, H., and Fox, K. R., *Rayon Textile Monthly*, **24**, 235 (1943).
- (38) Hoffman, R., and Beste, L., *Textile Research J.*, **21**, 66 (1951).
- (39) International Standards Organization.
- (40) Kaswell, E. R., *Textile Research J.*, **16**, 413, 502 (1946).
- (41) Kaswell, E. R., *Textile Fibers, Yarns and Fabrics*, Reinhold, N.Y., 1953. Figures 1 and 2 courtesy Reinhold Publishing Corp.
- (42) Leaderman, H., *Elastic and Creep Properties of Filamentous Materials and Other High Polymers*, The Textile Foundation, Washington, D.C., 1943.
- (43) Lehnicke, D. J., *Am. Dyestuff Repr.*, **38**, P853 (1949).
- (44) Lindberg, J., and Gralen, N., *Textile Research J.*, **18**, 287 (1948).
- (45) Maillard, F., *J. Textile Inst.*, **40**, 379 (1949).
- (46) Marsh, J., *Textile Inst.*, **22**, T245 (1931).
- (47) Martin, A., and Middleman, R., *J. Textile Inst.*, **37**, T269 (1946).
- (48) Medley, J., *J. Textile Inst.*, **45**, T123 (1954).
- (49) Mercer, E. H., and Makinson, K. R., *J. Textile Inst.*, **38**, T227 (1947).
- (50) Meredith, R., *J. Textile Inst.*, **36**, T107 (1945).
- (51) Meredith, R., *J. Textile Inst.*, **37**, 469 (1946).
- (52) Meredith, R., "Properties Depending on the Amorphous Regions of Fibres," in *Fiber Science*, J. M. Preston, ed., The Textile Institute, Manchester, 1949.
- (53) *Modern Plastics Encyclopedia*, Plastics Catalogue Corp., N.Y., 1949.
- (54) Morrow, J. A., *J. Textile Inst.*, **22**, T425 (1931).
- (55) Newell, W., "Synthetic Fiber Table," *Textile World* (Sept. 1951).
- (56) Painter, E. V., *Textile Research J.*, **22**, 153 (1952).
- (57) Peirce, F. T., *J. Textile Inst.*, **21**, T377 (1930).
- (58) Peirce, F. T., *J. Textile Inst.*, **28**, T45 (1937).
- (59) Platt, M. M., *Textile Research J.*, **20**, 1 (1950).
- (60) Platt, M. M., Hamburger, W. J., et al., Textile Series Reports, Office of the Quartermaster General, Washington, D.C.
- (61) Pollitt, J., *J. Textile Inst.*, **40**, P11 (1949).
- (62) Preston, J. M., *Modern Textile Microscopy*, Emmot & Co., Ltd., London, 1933.
- (63) Preston, J. M., ed., *Fibre Science*, The Textile Institute, Manchester, 1949.
- (64) Preston, J. M., *J. Textile Inst.*, **40**, T767 (1949).
- (65) Preston, J. M., *J. Textile Inst.*, **41**, P679 (1950).
- (66) Preston, J. M., and Ninkar, M. V., *J. Textile Inst.*, **40**, P674 (1949).
- (67) Ray, L., *Textile Research J.*, **22**, 144 (1952).

- (68) Rees, W. H., *J. Textile Inst.*, **32**, T149 (1941).
- (69) Rowen, J., and Gagliardi, D., *Am. Dyestuff Repr.*, **36**, 533 (1947).
- (70) Schiefer, H., et al., *J. Research Natl. Bur. Standards*, **32**, 261 (1944).
- (71) Schiefer, H., Fourt, L., and Kropf, R., *Textile Research J.*, **18**, 18 (1948).
- (72) Schwarz, E. R., *Textiles and the Microscope*, McGraw-Hill, N.Y., 1934.
- (73) Schwarz, E. R., *Textile Research J.*, **9**, 216 (1939).
- (74) Schwarz, E. R., "Textile Testing," in Matthews' *Textile Fibers*, 5th ed., H. R. Mauersberger, ed., Wiley, N.Y., 1947.
- (75) Sieminski, M. A., *Rayon Textile Monthly*, **24**, 585 (1943).
- (76) Smith, H. DeW., *Am. Soc. Testing Materials Proc.*, **44**, 543 (1944).
- (77) Speakman, J. B., and Stott, E., *J. Textile Inst.*, **22**, T339 (1931).
- (78) Susich, G., and Backer, S., *Textile Research J.*, **21**, 482 (1951).
- (79) Teixeira, N., and Edelstein, S., *Am. Dyestuff Repr.*, **43**, P195, (1954).
- (80) Thomson, R. H. K., and Traill, D., *J. Textile Inst.*, **38**, T43 (1947).
- (81) U.S. Government, "General Textile Federal Specifications CCCT 191-b," 1953.
- (82) Vogt, W. W., *Ind. Eng. Chem.*, **20**, 302 (1928).

ERNEST R. KASWELL

## THALLIUM AND THALLIUM COMPOUNDS

Thallium, Tl, atomic number 81, atomic weight 204.39, lies in group IIIB of the periodic table between mercury and lead. Several isotopes of thallium are known. The two stable, naturally occurring isotopes are  $\text{Tl}^{203}$  and  $\text{Tl}^{205}$ , which together constitute virtually all of the naturally occurring element. Small amounts of four radioactive isotopes occur in natural radioactive series as decomposition products. Other radioactive isotopes have been prepared artificially.

Thallium was discovered in 1861 almost simultaneously by A. Lamy and W. Crookes. Both discoveries were made by the observation of a previously unnoted spectral line in the bright green. From this W. Crookes named the element with the Latin word "thallus," green branch. The discoverers found the element in the examination of sulfuric acid plant residues. Lamy was apparently the first to isolate the metal, but much of the original work on its chemical properties was published by Crookes.

The chief valence number of thallium is +1. Less numerous and less stable compounds with the valence number +3 are known. It is calculated that thallium constitutes about 0.0003% of the earth's crust.

### PHYSICAL AND CHEMICAL PROPERTIES

Thallium metal is a little softer than lead and, when freshly melted and chilled, is almost as white as tin. However, the metal oxidizes superficially with great rapidity and acquires first a gray and then a brown-black coating of oxide. Some producers cover the rods of metal with paraffin to protect against oxidation.

**Constants.** The metal has two crystal forms,  $\alpha$ , stable at room temperature, and  $\beta$ , stable above 230°C. The crystal structure of  $\alpha$ -thallium is close-packed hexagonal (lattice constants:  $a = 3.450$ ,  $c = 5.514$ , kX units).  $\beta$ -Thallium has a body-centered cubic structure ( $a = 3.874$ ). The properties of the metal are: m.p. 303.5°C., b.p. 1460°C.; sp.gr. 11.85; specific heat at 20°C., 0.031 cal./(g.)(°C.); latent heat of fusion, 7.2 cal./g.; coefficient of linear thermal expansion,  $28.0 \times 10^{-6}$ ; electrical resistance at 0°C.,  $18 \times 10^{-6}$  (ohm)(sq.cm.)/(cm.); normal electrode potential 0.338 volt.

**Reactions.** Thallium metal is quite reactive chemically but appears somewhat inert because most compounds form coatings over the surface which interfere with complete attack. Mixed steam and air will react with the metal completely to produce a solution of thallos hydroxide. Thallium reacts with hot alcohol to form an ethoxide. The halogen acids produce only limited attack because of the insolubility of the resulting halides. Nitric acid acts readily on the metal to produce thallos or thallic compounds, according to its concentration. Hot, moderately concentrated sulfuric acid reacts with the metal effectively, giving thallos sulfate.

#### ANALYSIS

Thallium may be detected on a macro scale by precipitation of thallos iodide. The flame test is very sensitive. Micro quantities of thallium may be detected or determined by the use of thionalide (2-mercapto-*N*-2-naphthylacetamide). This reagent is claimed to be specific for thallium in solutions containing sodium hydroxide, sodium tartrate, and sodium cyanide. For a macro determination, a number of methods are available, of which precipitation and weighing as thallos chromate is preferred.

#### OCCURRENCE AND PRODUCTION

The commercial sources of thallium are flue dusts, either from pyrites burners or from lead and zinc smelters and refiners. In these dusts the thallium occurs largely as sulfate or other compounds, which are extracted by hot water, sometimes with the addition of acid. Crude thallium is isolated from the extracts by precipitation as metal onto zinc or aluminum or by precipitation as chloride, which can be recrystallized from dilute sulfuric acid for purification. Electrolysis of carbonate, sulfate, or perchlorate solutions is another method for isolation of thallium metal.

**Economic Aspects.** No figures are available for the domestic production or consumption of thallium as metal or its compounds. It is believed that this is in the range of 5,000–10,000 lb. per annum with the probability nearer the lower figure. The price of the metal for some years has been \$12.50 per lb., and of thallos sulfate \$10.50 per lb.

#### ALLOYS AND APPLICATIONS

No uses have been found for thallium metal *per se*. A considerable number of alloys are known, some of which have useful properties. Almost all the binary alloys of thallium with the major metallic elements have been made and studied. With the exception of copper, aluminum, arsenic, manganese, nickel, and selenium, free alloying occurs. Thallium is only slightly soluble in either molten or solid copper, aluminum, zinc, and nickel. In this it resembles lead. The lead alloy is peculiar (see below). With mercury, thallium forms an intermetallic compound melting at 145°C. Compositions on either side of this compound tend to eutectics of which one with 40.50% Tl melts at 0.6°C. and the other, which has been proposed for use in low-temperature thermometers, contains 8.9% Tl and melts at -60°C.

A number of ternary alloys have been studied. The addition of 6% thallium to Lipowitz metal (see Vol. 2, p. 531) lowers the melting point from 70° to 66.6°C. It is claimed that the addition of thallium to lead and to lead alloys increases the resistance to deformation, the yield point, and the ultimate strength.

Thallium-lead alloys have higher melting points than either component and are harder. They also possess increased resistance to atmospheric or anodic corrosion.



For these reasons they are recommended as anodes for the electrolytic deposition of copper, as high-temperature solders, and as electric fuse metal.

A silver-thallium bearing alloy is especially good for its antiseizing properties and has better antifriction properties and lower corrosion rates than analogous silver-lead and copper-lead alloys. The addition of 0.5–5.0% thallium to gold or silver for electrical contacts is claimed to decrease the tendency of these to stick. An alloy of silver (min. 78%) with aluminum (0.3–20%) and thallium (0.3–18%) has been suggested for stainless silverware. Applications of thallium to equipment for the food industries are, of course, barred on account of the poisonous nature of thallium.

### Thallium Compounds

#### Thallium Halides.

The water solubility of the thallous (thallium(I)) halides decreases regularly from the fluoride to the iodide. **Thallous fluoride** is prepared by reaction of thallous carbonate with hydrofluoric acid. **Thallous chloride, bromide, and iodide** are prepared by precipitation from boiling solutions of the sulfate with dilute solutions containing the required ion. The chloride may be recrystallized from boiling water, but the bromide and iodide are too insoluble to permit this. The three common halides are all light-sensitive and must be kept in the dark to preserve them.

**Thallic fluoride** (thallium(III) fluoride) can be prepared by the reaction of fluorine with thallic oxide. It reacts instantly with moisture and is decomposed by heating in air. Thallic chloride and thallic bromide are difficult to prepare in anhydrous condition but may readily be prepared as hydrated crystals containing  $4\text{H}_2\text{O}$ . To prepare **thallic chloride**, thallous chloride is suspended in boiling water and chlorine passed in until complete solution has taken place and an excess of chlorine is evident. The solution is evaporated at  $60\text{--}70^\circ\text{C}$ . on a water bath while chlorine is passed in continuously. When the concentration has proceeded to the point of a thin sirup, the mixture will crystallize in an ice bath. The crystals can be pressed dry and then dried for 24 hours over sulfuric acid and potassium hydroxide. **Thallic bromide** is prepared analogously except that the temperature of evaporation is preferably kept below  $40^\circ\text{C}$ . To avoid supersaturation a part of the concentrated solution may be chilled rapidly by dry ice to produce seed crystals. Anhydrous thallic chloride is prepared by dehydration of the hydrated crystals with thionyl chloride. Thallic chloride lends itself readily to the preparation of a number of coordinated complexes which include *tetrachlorothallic(III) acid*,  $\text{H}(\text{TlCl}_4) \cdot 3\text{H}_2\text{O}$ ; *thallium(I) tetrachlorothallate(III)*,  $\text{Tl}(\text{TlCl}_4)$ ; *thallium(I) hexachlorothallate(III)*,  $\text{Tl}_3(\text{TlCl}_6)$ ; and analogous salts of alkali metals. Especially to be noted are *potassium pentachloromonoaquothallate(III)*,  $\text{K}_2(\text{TlCl}_5\text{H}_2\text{O}) \cdot \text{H}_2\text{O}$ , and *cesium nonachlorodithallate(III)*,  $\text{Cs}_3(\text{Tl}_2\text{Cl}_9)$ . Thallic bromide forms a similar series of compounds. In the case of *thallic iodide* there seems to be some question whether the compound is truly a derivative of trivalent thallium or merely one of the usual triiodides with the formula  $\text{TlI} \cdot \text{I}_2$ .

#### Thallium Oxides and Hydroxide.

**Thallous oxide** is a black crystalline material which begins to sublime at  $300^\circ\text{C}$ . in high vacuum, although its boiling point is at least  $1080^\circ\text{C}$ . It is gradually attacked by water with the formation of thallous hydroxide and dissolves in absolute alcohol to

some extent to form thallos ethoxide. It is prepared by exhaustive drying of the hydroxide in high vacuum at 50°C. At higher temperatures some peroxide is formed. **Thallic oxide** is a brown to black powdery material which is difficult to prepare in an anhydrous condition. The hydrated oxide is formed readily by hydrolysis of thallic compounds, and by repeated washing can be freed entirely from acids. On drying, however, it clings tenaciously to the last traces of water, and it is claimed that some decomposition to lower oxides occurs before dehydration is complete.

The classical preparation of **thallous hydroxide** is by decomposition of the ethoxide with water. The ethoxide is formed from the metal by the action of hot ethyl alcohol in the presence of air. *Thallos ethoxide*,  $\text{TlOC}_2\text{H}_5$ , separates from the alcohol on cooling as a heavy oil, usually containing some hydroxide. Approximately an equal volume of freshly boiled and cooled water is added, and the alcohol formed is removed by evacuation. A more direct process is to pass a mixture of steam and air ( $\text{CO}_2$ -free) over mossy thallium in a column. The solution of thallium hydroxide which drips from the column is concentrated and the crystals dried *in vacuo*. The crystals are pale yellow but readily become dark because of decomposition to the oxide. They are readily soluble in water and the solution is strongly alkaline so that when hot it will even attack glass.

### Thallium Sulfates.

**Thallos sulfate** is commercially available. It is readily formed by reacting metallic thallium with hot dilute sulfuric acid and evaporating the solution to crystallization. A more rapid process is to react the thallium with hot concentrated sulfuric acid and to recrystallize from water after cooling the solution. A normal thallium(III) sulfate cannot be isolated as the compound hydrolyzes very readily. However, under proper conditions a **basic thallic sulfate** of a composition  $\text{Tl}(\text{OH})\text{SO}_4 \cdot 2\text{H}_2\text{O}$  can be prepared and crystallized from 20% sulfuric acid. From a more concentrated sulfuric acid a **disulfatothallic acid**,  $\text{HTl}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$ , crystallizes.

Of the many other compounds which thallium forms, including a series of sulfides and selenides, a nitride, a nitrate, and a carbonate, the only ones which are not mere curiosities are the **formate** and the **malonate**. These have the property that a saturated solution of the two in approximately equal weights gives an aqueous solution with specific gravity as high as 4.324 at 20° and so is useful in mineralogical analysis. The component salts can readily be prepared from thallos carbonate by reaction with the appropriate acid.

### USES OF THALLIUM COMPOUNDS

The major use of thallium is as the sulfate for rodenticides and insecticides. A paste of thallos sulfate, which must be neutral, starch, sugar, glycerin, and water is applied to bread crumbs or wheat grains. As the thallium salt is odorless and tasteless, it gives no warning to the rats. An ant poison is made as a sirup containing 1 oz. thallium sulfate, 6 lb. sugar, 18 oz. honey, and 6 pt. water. See *Poisons, economic*.

"Thallofide" cells containing thallium oxysulfide as the photosensitive agent and made by thermal evaporation of thallos sulfide in oxygen at 0.8 mm. are used for the detection of long-wave (infrared) radiation (see *Photoelectric cells*). They are more sensitive than selenium cells in this application. For war communications the thallium sulfide photocell has been further developed to improve stability and sensitivity

and to eliminate the time lag in attaining full response to signals. It is found that the degree of oxidation is a controllable variable of considerable effect for most efficient action.

Biochemists have done considerable research on the unusual physiological properties of thallium salts. Thallous acetate has been used medicinally for the treatment of dysentery and of tuberculosis. It has also been used dermatologically for ringworm and other skin affections. At one time a cosmetic depilatory based on thallous acetate was sold. This, however, met with financial disaster when many users were poisoned by skin absorption and sued the producing company. In general, the medicinal use of thallium compounds has been limited probably to the vanishing point by their poisonous properties. Thallous carbonate has been used to waterproof, mothproof, and mildewproof textile fabrics. Thallium compounds in glass result in a higher refractive index than that of lead glass, and this property has led to some use for optical glass and for rhinestones.

Thallium and thallium-vanadium catalysts are proposed for catalytic reductions and sulfuric acid oxidation, respectively.

A relatively new use for thallium compounds which shows promise of growth derives from the infrared transmission of the mixed bromide-iodide crystals. Crystals with 42 mole per cent thallous bromide and 58 mole per cent thallous iodide have a transmission of approximately 67% from 10–14 $\mu$ . The crystals are grown from a

TABLE I. Properties of Some Thallium Compounds.

Compound	Color and crystal form	Solubility, parts per 100 parts solvent		
		Cold water	Hot water	Other reagents
Thallium acetate, $\text{TlC}_2\text{H}_3\text{O}_2$	silky needles	v.s.	—	v.s. alc.
" carbonate, $\text{Tl}_2\text{CO}_3$	white, monoclinic	4.2 <sup>15°</sup>	27.2 <sup>100°</sup>	—
" chromate, $\text{Tl}_2\text{CrO}_4$	yellow crystals	0.03 <sup>100°</sup>	0.2 <sup>100°</sup>	sl.s. a., alk.
" chloride, $\text{TlCl}$	white, cubic	0.21 <sup>10°</sup>	1.8 <sup>100°</sup>	sl.s. HCl
" chloride, $\text{TlCl}_3$	hex. plates	v. s.	—	sol. alc., et.
" bromide, $\text{TlBr}$	yellow, cubic	0.024 <sup>10°</sup>	0.257 <sup>10°</sup>	—
" bromide, $\text{TlBr}_3 \cdot 4\text{H}_2\text{O}$	yellow, deliq.	sol.	v.s.	v.s. alc.
" fluoride, $\text{TlF}$	col., cubic	80.15°	v.s.	sl.s. alc.
" fluoride, $\text{TlF}_3$	olive green	i.	—	i.e. HCl
" oxide, $\text{Tl}_2\text{O}$	yellow deliq.	v.s.	v.s.	—
" oxide, $\text{Tl}_2\text{O}_3$	blk. or brn., hex.	i.	i.	sol. a.; i. alk.
" sulfate, $\text{Tl}_2\text{SO}_4$	col., rhombic, 1.8671	2.70 <sup>10°</sup>	18.45	—
" sulfide, $\text{Tl}_2\text{S}$	blk.	0.022 <sup>20°</sup>	sl. s.	s. alc.; i. alk.

a. = acids  
alc. = alcohol  
alk. = alkalies  
blk. = black

brn. = brown  
c. = cold  
col. = colorless  
deliq. = deliquescent

et. = ether  
hex. = hexagonal  
i. = insoluble  
sol. = soluble  
sl. s., v.s. = slightly soluble,  
very soluble

melt according to now common procedures. Windows, lenses, and prisms can be ground from the crystals for use in infrared detection and measuring devices. As little as 0.1% of thallous iodide in a melt of sodium iodide gives the product the property of converting energy from various radioactive substances to light photons which can be detected by a sensitive photomultiplier tube. Hence the use of this composition in scintillation counters.

## Bibliography

- (1) Donges, E., in Brauer (ed.), *Handbuch der präparativen anorganischen Chemie*, Enke, Stuttgart, 1952.
- (2) Gmelin, System No. 38 (only part of this volume has been printed).
- (3) Howe, H. E., and Smith, A. A., Jr., *J. Electrochem. Soc.*, **97**, No. 8, 167-70C (Aug. 1950).
- (4) Sidgwick, N. V., *The Chemical Elements and Their Compounds*, Oxford Univ. Press, London, 1950, Vol. I, pp. 458-488 (185 references).
- (5) Waggaman, W. H., Heffner, G. G., and Gee, E. A., "Thallium," *U.S. Bur. Mines Inform. Circ.*, 7533, March, 1950 (369 references).

KARL M. HERSTEIN

**THEBAINE**,  $C_{19}H_{21}NO_3$ ; **THEBAINONE**,  $C_{18}H_{20}NO_3$ . See *Alkaloids*, Vol. 1, p. 493.

**THEELIN**,  $C_{18}H_{22}O_2$ ; **THEEOL**,  $C_{18}H_{24}O_3$ . See *Hormones (sex)*, Vol. 7, pp. 519, 524.

**THEINE**,  $C_8H_{10}N_4O_2$ . See *Caffeine*.

**THENYLPYRAMINE HYDROCHLORIDE**,  $C_{14}H_{19}N_3S \cdot HCl$ . See *Histamine and antihistamine agents*, Vol. 7, p. 471.

**THEOBROMINE**,  $C_7H_8N_4O_2$ . See *Alkaloids*, Vol. 1, p. 474; *Chocolate*, Vol. 3, p. 915; *Diuretics*, Vol. 5, p. 191.

**THEOPHYLLINE**,  $C_7H_8N_4O_2 \cdot H_2O$ . See *Alkaloids*, Vol. 1, p. 475; *Diuretics*, Vol. 5, p. 190.

## THERMAL ANALYSIS

Thermal analysis was developed to meet the need for a means of determining the nature and character of certain minerals and mixtures of minerals, or detecting minor transformation points in metals. Such characteristics are not revealed by either chemical analysis or x-ray diffraction techniques. The differential method of conducting thermal analysis consists essentially of plotting the temperature of the specimen under investigation against the difference in temperature between the specimen and a neutral body.

For example, the application of heat to many minerals causes certain physical and chemical changes that are reflected in endothermic or exothermic reactions. Since the sample to be analyzed and a thermally inert standard are both heated equally, the heat input of the furnace is neglected, and only the anomalous temperatures in the sample are indicated as peaks of endothermic or exothermic changes. Since an exothermic reaction of a mineral gives it a higher temperature than that of the inert standard, an upward deflection of the thermal analysis curve takes place. A downward deflection is evident when the temperature of the specimen becomes lower than that of the standard. When a transformation point in a sample is reached, the uniform change in the specimen is temporarily arrested, whereas the temperature of the neutral body continues to change with practically no interruption. Thereby minor transformations are detected easily. See also *Melting and freezing temperatures*; *Phase rule*; *Thermochemistry*; *Thermodynamics*.

In describing thermal analysis curves, certain conventions are followed:

(1) Peaks are upward or downward deflections from a straight line. As obtained with conventional apparatus, the endothermic peak is downward, and an upward de-

deflection is exothermic. (2) Temperature defines the furnace environment and is described by the horizontal displacement along the thermal curve. (3) The vertical extent of the peak is the differential temperature between two materials in the furnace and is defined by its relative height. (4) The area of the peak is that area included by the actual curve and a line joining the two points where deflection begins and ends.

A thermal analysis technique was originally proposed by Le Chatelier in 1887 to aid in the qualitative identification of clay minerals. The method of thermal analysis was first applied to clays when Le Chatelier studied the thermal characteristics of alumina silicates and attempted to classify them by this means. In 1913, similar work was carried out by Wallach, who indicated that certain minerals could be identified by their thermal behavior. Satoh also used the method for investigating various kaolins in 1921. Mellor and Holdcroft, in 1911, demonstrated the endothermic and exothermic effects characteristic of kaolinite and a wide range of other clay materials.

Houldsworth and Cobb (8) were the first to apply the method of differential thermal analysis, in which the temperature of the test material was measured relative to that of an adjacent inert material, rather than to that of the furnace employed. Thermocouples embedded in the test sample and inert material were connected in opposition, so that any appreciable electromotive force set up during the heating resulted from the evolution or absorption of heat in the test sample.

From about 1935 on, the method gained favor and began to be increasingly applied in mineralogical studies of clays and related silicates. For example, clays, laterites, bauxites, and montmorillonite minerals were investigated by Orzel (17,18). Insley and Ewell (9) studied kaolin minerals, and Ewell and co-workers (3) investigated talc. Thilo and Schumemann (23) obtained curves of pyrophyllite. Norton's work in 1939 illustrated the possibilities of an improved method for identifying and estimating clay minerals (15). Since Norton, the method has received considerable attention by clay mineralogists (4,11,12), soil technologists (2,6,10,19), ceramists (14), and metallurgists.

Gradual refinements and modifications have broadened the general field of application to cover a multitude of problems. Smothers (22) has compiled an extensive bibliography of the differential thermal analysis literature.

### Theory

Because different substances possess dissimilar amounts of energy, the total energy of the products of a reaction may diverge from the total energy of the reactants. Consequently, a process is usually accompanied by an absorption or liberation of energy in the form of heat. On the other hand, a thermally inert material exhibits the temperature of its environment at all times, if the small lag caused by the conductivity of a sample is neglected. Therefore, when any reactions which absorb or emit heat take place in a material, the material fails to maintain continuous thermal equilibrium with its environment. Momentarily the temperature may be above or below that of the inert sample experiencing the same temperature rise, and observations of these heat changes become convenient indexes of the reactions.

Cooling and heating curves have been used in some mineral studies with no appreciation of the difference between reversible and irreversible chemical changes. It is inadmissible to use a method of cooling to evaluate an irreversible thermal change that occurs only with rising temperature. It is well known that most of those changes undergone by minerals, silicates, and materials of ceramic importance are not reversed by cooling. Any method of treating mixtures with irreversible reactions by quenching the specimen cannot evaluate the heats of reaction.

The maximum temperature difference between a thermally active material and its environment is a function of the mass, specific heat, thermal conductivity, and the heat liberated or absorbed by the reaction. If an inert material occurs in the active

sample, it may act as a diluent; its mass, specific heat, and conductivity also affect the net thermal curve. In some mixtures, a reaction of one material can mask out that of another constituent. Consequently, the total heat transfer depends upon the environment, the nature of the reactants, and the thermal conductivity of the gas present in the sample.

**Thermal conductivity** of dissimilar minerals is known to vary over reasonably wide ranges, but values given by Baver (1) show that dry compacted kaolin has a relative heat conductivity differing by only 25% from quartz powder similarly compacted. Work by Smith and Byers (20) shows that the thermal conductivity varies only slightly with soil constituents. Since Gruver (5) found that degree of packing is unimportant, it means that the gaseous environment is important. For powders and porous substances, thermal conductivity is a function of the gas temperature in the pore structure. The conductivity curves of highly porous materials with the continuous air type of structure exhibit a minimum when plotted as a function of porosity.

For most minerals the **specific heat** in calories per gram is around 0.18 to 0.25, as compared to 1.0 for water. Therefore, variations in absorbed moisture may influence very materially the heating rate of a sample over the low temperature region and may produce anomalous endothermic effects. When a hydrous material is packed into a container in such a manner that the pore spaces are not interconnected, the evolved water may remain interstitially and absorb more energy before being driven off.

It is assumed in differential thermal analysis that the properties are uniform throughout the sample. This is not true, because a thermocouple must be inserted at the center of the sample to measure the temperature, and heat flow along the thermocouple wires tends to equalize the temperature differential more rapidly. For this reason, the use of small thermocouple wires is recommended. The thermocouple junctions also should contain as little metal as possible. They should have essentially no bead, and both thermocouples should stand at a uniform height. Otherwise, the thermocouples will not absorb and release heat in the same manner.

### Equipment

Design of the container for the sample and for the inert reference body is important. The ideal condition would be to suspend sample and reference in an infinite heat reservoir. Because this is impractical, a thin-walled cylinder may be used to contain each mass. Tests along such lines by Herold and Planje (7) indicate that such a design improves the response of the thermocouple. The crucibles that were used by Herold and Planje were also integral parts of the thermocouples and allowed extension of the temperature range to 1600°C.

Another alternative for approaching the infinite heat reservoir has been to go to the other extreme of increasing mass and conductivity of the container, so that the holder itself approaches the condition of an infinite heat reservoir. Nickel achieves this condition quite readily, but it oxidizes, and the surface becomes reticulated so that poor heat transfer results. Large thermal gradients then develop because of the poor thermal junction between metal container and sample. A block of beryllium oxide may be considered as useful for container material because of its thermal conductivity and electrical insulation characteristics.

A cross section of a typical thermal analysis furnace is shown in Figure 1. The

block is formed from sintered alumina or beryllia with two cavities to receive metallic cups. The metallic cups form the differential thermocouple. The upper portions of the cups and connecting leads are formed from one metal (platinum), and the lower portions of the cups with extension leads are of the other metal (platinum-10% rhodium). The cups are charged with the sample and inert standard and are placed in the furnace laterally rather than longitudinally. This position assures the same heat input to each throughout the entire run. The temperature of the block is measured by a separate thermocouple imbedded in the center of the ceramic block. This arrangement eliminates complications of temperature measurement and gives temperatures that do not deviate more than a few degrees from the temperature of the sample. In fact, a temperature taken in the block itself is more suitable for a base than the temperature of the neutral body, since the body may show temperature fluctuations due to shifts in the couple position.

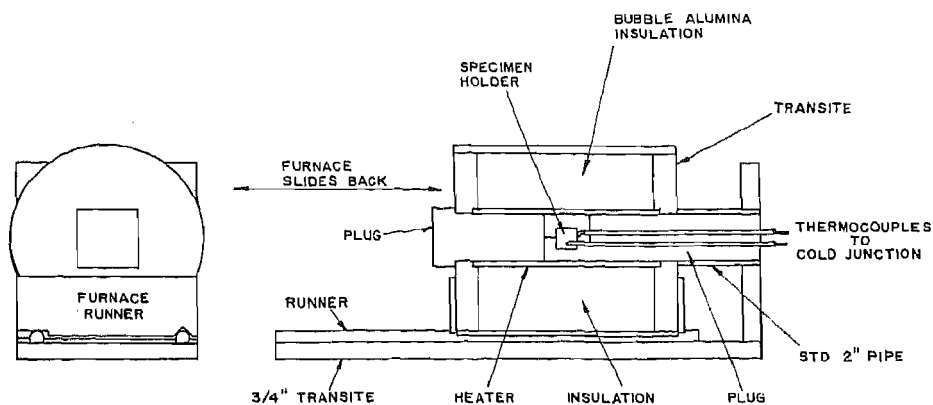


Fig. 1. Cross section of thermal analysis furnace.

The differential temperature is read with a recording galvanometer of such a resistance that no shunt is required. A continuous record may be produced on a strip of photographic paper with the actual temperatures recorded on the same sensitive paper by a signal lamp that is flashed every time the potentiometer reading comes to an even 50-degree interval. The rate of temperature rise is preset by a program controller. The voltage applied to the furnace comes from an automatically controlled Variac which increases or decreases the power by the position of the control galvanometer. A carry motor turns the program cam, which, in turn, uniformly increases the millivolt setting of the control dial. The setting is compared to the furnace temperature by means of the thermocouple connection so that an increase or decrease over the desired rate develops a signal error which is fed to the Variac motor.

The timing motor, along with the recorder, provides an exposure of the 50-degree signal line on the differential plot photograph. When a 50-degree potential is reached, the recorder unit energizes the timing motor through closed contacts of the thermal relay. The timing motor turns, instantly closing a microswitch which serves to keep the timing motor running for one half a revolution. As the timing motor rotates, another microswitch in the 50-degree signal circuit closes to energize the 50-degree signal light that produces the 50-degree signal line on the thermal curve plot. After one half a revolution, the first microswitch opens to stop the motor in a position readied

for the next operational sequence. The time of contact of the 50-degree signal switch may be varied for every other line signal to give a heavier line every 100 degrees.

The differential thermocouple records the thermal reactions by means of a mirror galvanometer that reflects a light beam from a continuous source of light. All variations in the thermocouple potential change the position of the mirror and hence the position of the beam reflected onto the photographic paper. A photoelectric potentiometer may be substituted for the galvanometer box and drum of photosensitive paper. Such an instrument is very fast and very sensitive from 0.2 d.c. millivolts to 50 d.c. millivolts. Only one half second is required for full-scale deflections that can be observed as they develop. This is a distinct advantage over the light-sensitive paper method which requires loading, unloading, and developing in a dark room. McConnell and Earley (13) give an excellent description of a completely electronic device for obtaining thermograms. A preamplifier receives the d.c. signals directly from the differential thermocouple and amplifies the signals to suitable levels for the recorder. The range of the preamplifier may be changed by means of a dial that permits full-scale recording on a 10-inch chart for 50, 100, 200, 500, 1000, or 2000 microvolts. A chart speed on the recorder of 12 inches per hour permits very accurate determinations of the deflection temperatures, and a chart speed of 4 or 6 inches per hour produces a curve with conventional proportions that can be reproduced by tracing or photographic methods. Many other recording devices are also known.

The furnace is made of an alumina muffle wound with resistance wire. The shell is a cylinder of galvanized sheet iron. The end pieces are of asbestos board, and the space between the muffle and shell is filled with calcined diatomite or bubble alumina. The ends of the muffle are closed with plugs cut from insulating firebrick and coated with high-alumina cement. A groove cut along the top of the plugs supports the couple holders. The furnace slides on runners to allow the specimen block to be exposed for changing samples without disturbing the thermocouple connections.

### Types of Qualitative Curves

At least five types of deflections of the differential curve have been noted. These curves are: (1) the broad, low-amplitude endothermic characteristic of the low-

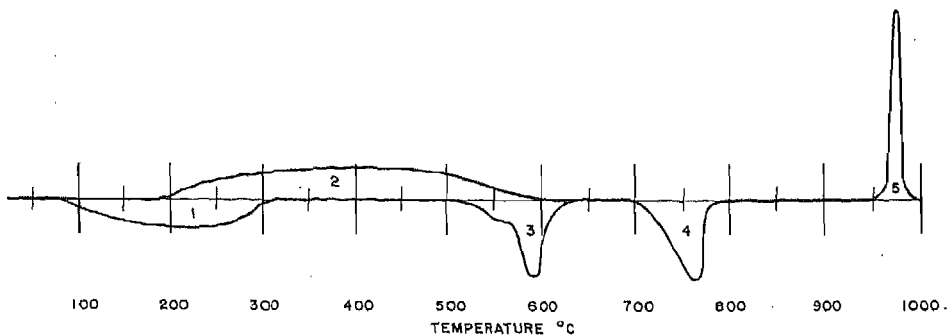


Fig. 2. Composite thermal curves.

temperature removal of absorbed water between 100 and 300°C.; (2) the broad asymmetrical exothermic deflection of the ball clays caused by the oxidation of organic matter between 200 and 600°C. (a sharp exothermic reaction between 400 and 500°C.



indicates pyrite or marcasite); (3) the symmetrical large-amplitude, broad-based deflection characterized by the endothermic removal of lattice water between 450 and 700°C.; (4) the asymmetrical large endothermic deflection typical of the carbonates occurring anywhere between 450 and 900°C. and depending upon the carbonate; and (5) the narrow-temperature-range, high-amplitude exothermic peak of the kaolin minerals.

A composite curve of these broad categories is shown in Figure 2. This curve represents no particular mineral.

Thermal curves for the kaolin minerals are illustrated in Figure 3. All of the kaolin minerals are characterized by an endothermic area at approximately 600°C., caused by hydroxyl groups breaking down in the crystal structure. At 980°C., an exothermic peak occurs that corresponds to the transformation of amorphous alumina

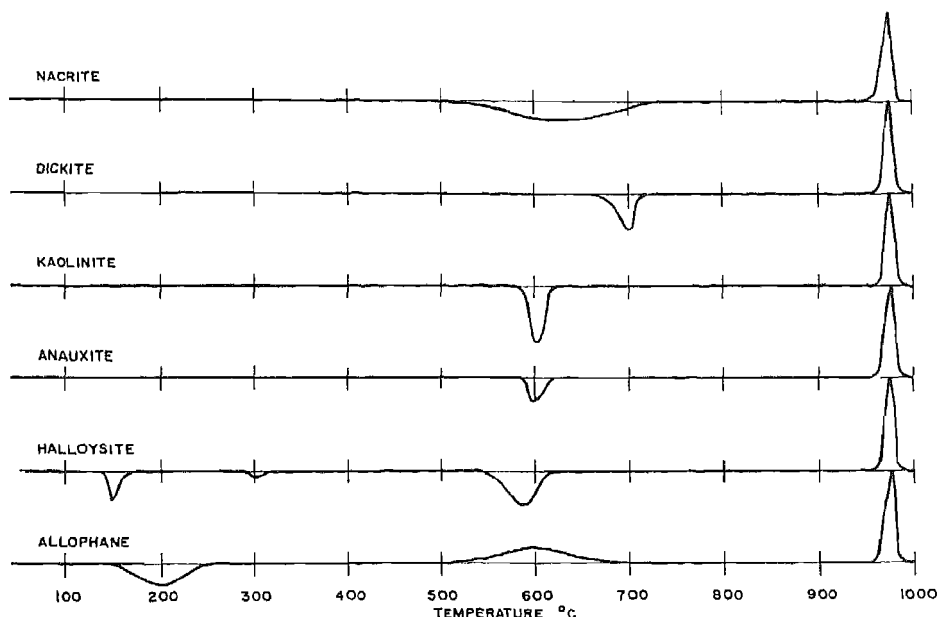


Fig. 3. Thermal analysis curves of kaolin minerals.

to  $\gamma$ -alumina. Thermal curves of nacrite, dickite, and kaolinite show only small deviations from a straight line in the initial portions of the plot. The deviations are caused by minute amounts of adsorbed moisture. The illustrations of Figure 3 indicate that it is possible to distinguish definitely between the three kaolin minerals—nacrite, dickite, and kaolinite. Anauxite exhibits a curve similar to kaolinite, except for a slightly smaller area under the endothermic peak. Halloysite can be distinguished readily from the other kaolin minerals because of two low-temperature peaks that are sharp and distinct at 150 and 325°C. Allophane is of such fine grain size that it is *sometimes considered amorphous*. The mineral exhibits a large endothermic effect at 180°C., but the base extends over a wide range.

Montmorillonite minerals are believed to possess a symmetrical sheet structure similar to that of pyrophyllite. Montmorillonite is characterized by a strong double peak at low temperatures that is very characteristic of the mineral. Talc gives a

distinct endothermic peak at 990°C. The relatively high temperature of this main endothermic peak is evidence of the great strength that the OH bonds have in this crystal structure. Gibbsite exhibits a large heat absorption at 350°C. that is expected because of the high chemical water content (twice that of kaolin minerals). Diaspore gives a single definite peak at approximately 550°C.

Occasionally, instrument difficulties, such as poor contacts, will produce spurious deflections in the thermogram. A little experience on the part of the investigator will enable him to recognize a deflection caused by improper functioning of the equipment. One reliable criterion is available. Any noticeable departure from linearity of the time-temperature curve should have a concomitant effect on the differential thermal analysis curve.

### Quantitative Analysis

Quantitatively, an area under a curve is a measure of the total heat effect; thus, this area is proportional to the amount of thermally active material. The measurement of the quantity of any one substance in a mixture is carried out by first determining which substance it is, and then measuring the area under the selected peak. This area, when divided by a standard area obtained by analyzing the pure substance, with the same equipment, gives the ratio of the constituents in a mixture.

In the quantitative measurement of heat effect there are several factors which influence the results. The most important of these are given below.

**Packing** (the physical characteristic of the sample when packed in the test cavity). It has been thought that the denser the packing, the sharper the heat effect appeared. Gruver (5), on the other hand, shows evidence that the manner in which a sample is packed into the holder has little effect on the area or intensity of the curve.

**Thermocouples** (the position and thermal capacity of the thermocouples). These elements should be centered in the sample. Fine wires (22-gage) have been found to work best because thermocouples, being excellent conductors of heat, have a marked effect upon the sensitivity of the method. The influence of the wire is felt since the amount of sample is small. It is conceivable that the amount of heat liberated or absorbed by a sample during heating could be so small as to have virtually no effect upon a measuring thermocouple that has both high heat capacity and high thermal conductivity. Differential thermocouple wires should have a thermal capacity as low as practicable and should be as fine as possible.

**Particle Size.** A decrease in particle size decreases somewhat the reaction energy associated with differential thermal peaks. The standard range is from -60 to +200 mesh to improve the packing characteristics of the powder.

**Rate of Temperature Rise.** The heating rate affects the position and thermal peak of the thermal curve, but does not appreciably change the area under a peak. The peaks generally become sharper with increase in heating rate and occur at somewhat higher temperatures. Standard rate of heating is 10-15°C. per minute.

**Diffusivity.** A marked difference in diffusivity between the material being examined and the standard contributes to the drift observed in the base line. Where drift occurs, the establishment of a fiduciary base line is essential in the quantitative interpretation of thermal analysis results, and also may prove to be significant for qualitative data. Experience indicates that drift can be minimized by selecting a reference material with thermal characteristics approaching those of the test samples

as closely as possible. For this reason, some investigators prefer precalcined test material for the inert sample.

**Furnace Atmosphere.** The environment is particularly important when the samples contain organic substances. The ease of oxidation must be controlled both by the furnace atmosphere and by the packing of the powder. Thermal analysis of substances containing oxidizable materials should be carried out in a controlled atmosphere, so that interference from oxidation reactions can be eliminated. In every case where oxidation exists, the distortion (or even suppression) or migration of characteristic peaks is so much in evidence as to render identification very difficult. Compounds of iron, in particular, can confuse thermal analysis curves. Stone (21) describes an apparatus designed so that an atmosphere containing any partial pressure of active vapor, such as water, carbon dioxide, or other gases, can be maintained around the particles of mineral powder while the thermal analysis is being run. The differential thermal analysis curves for montmorillonite indicate that the 730°C. endothermic peak is much sharper in a flowing stream of steam than in dry air.

**Crucible Material.** In differential thermal analysis, the effect of heat capacity of the crucible material is very marked. Containers of high heat capacity (for example, nickel) act as heat reservoirs and quickly absorb thermal energy from the sample, or return heat to it. Thus the intensities of the peaks are reduced or may be completely blotted out. On the other hand, platinum crucibles, with very low heat capacities, are ideal for sensitive devices that detect very small thermal changes.

Thermal analysis curves serve both qualitatively and quantitatively as dynamic records, and not as static or equilibrium records of thermal reactions occurring within the sample being studied.

### Applications

Differential thermal analysis can be adapted in a novel way to the study of enamels. Five enamel frits with titanium oxide concentrations varying from 9.3 to 23.4% were analyzed by Olympia (16). Several significant features were observed from the thermograms. For example, unreacted silica in the frit was detected, the extent of formation of crystal nuclei was noted, and the point of fusion was determined. An exothermic peak on the curve was found to represent the formation of anatase.

The application of differential thermal analysis curves in a number of fields is increasing. Agricultural investigators utilize the method to analyze soils for chemically treated minerals; geologists use differential techniques to identify minerals and mineral aggregates; ceramists study clays (*q.v.*) and allied minerals of natural occurrence or of artificial preparation. In chemistry, the differential thermal analysis method is helpful in the investigation of soaps, phosphors, and phase changes in chemicals. In metallurgy, there is a consistently continuing study of transformations in phases and states. In fuel technology, coals have been studied very extensively; however, at present, more work is conducted in geological explorations for oil.

The thermal differential method is particularly valuable for identifying minerals when they occur in such a finely crystalline state that petrography or x-ray analysis is of little value. The thermal method of course does not supplant either of the other methods of analysis; it is an additional tool and should be a part of every research and control laboratory dealing with minerals.

## Bibliography

- (1) Baver, L. D., *Soil Physics*, Wiley, N.Y., 1940, p. 279.
- (2) Dean, L. A., *Soil Sci.*, **63**, 95 (1947).
- (3) Ewell, R. H., Bunting, E. N., and Geller, R. F., *J. Research Natl. Bur. Standards*, **15**, 551 (1935).
- (4) Grim, R. E., and Rowland, R. A., *Am. Mineral.*, **27**, 746-61, 801-18 (1942).
- (5) Gruver, R. M., *J. Am. Ceram. Soc.*, **31**, 323-28 (1948).
- (6) Hendricks, S. B., Goldich, S. S., and Nelson, R. A., *Econ. Geol.*, **41**, 64 (1946).
- (7) Herold, P. G., and Planje, T. J., *J. Am. Ceram. Soc.*, **31**, 20 (1948).
- (8) Houldsworth, H. S., and Cobb, J. W., *Trans. Brit. Ceram. Soc.*, **22**, 111 (1923).
- (9) Insley, H., and Ewell, R. H., *J. Natl. Bur. Standards*, **14**, 615 (1935).
- (10) Jeffries, C. D., *Soil Sci. Soc.*, **9**, 86 (1944).
- (11) Kerr, P. F., and Kulp, J. L., *Am. Mineral.*, **33**, 387 (1948).
- (12) Kulp, J. L., and Kerr, P. F., *Am. Mineral.*, **34**, 839 (1949).
- (13) McConnell, D., and Farley, J. W., *J. Am. Ceram. Soc.*, **34**, 184 (1951).
- (14) Nagy, R., and Chung, K. L., *J. Opt. Soc. Amer.*, **37**, 37 (1947).
- (15) Norton, F. H., *J. Am. Ceram. Soc.*, **22**, 54 (1939).
- (16) Olympia, F. D., *Bull. Am. Ceram. Soc.*, **32**, 412 (1953).
- (17) Ortel, J., *Compt. rend.*, **183**, 565 (1926).
- (18) Ortel, J., and Caillere, S., *Compt. rend.*, **197**, 774 (1933).
- (19) Schafer, G. M., and Russel, M. B., *Soil Sci.*, **53**, 353 (1942).
- (20) Smith, W. O., and Byers, H. G., *Soil Sci. Soc. Am. Proc.*, **13**, 3 (1948).
- (21) Stone, R. L., *J. Am. Ceram. Soc.*, **35**, 76 (1952).
- (22) Smothers, W. J., "Bibliography of Differential Thermal Analysis," *Univ. Arkansas Inst. Sci. and Technol. Research Ser.*, **21**, 44 (1951).
- (23) Thilo, E., and Schuneman, H., *Z. anorg. allgem. Chem.*, **230**, 321 (1937).

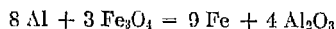
J. A. STAVROLAKIS

**THERMAL BLACK.** See *Carbon (carbon black)*, Vol. **3**, p. 46; *Pigments (inorganic)*, Vol. **10**, p. 652.

**THERMIONIC TUBES.** See *Electronics*, Vol. **5**, p. 558; *Vacuum tubes*.

## THERMIT PROCESS

The thermit, or Goldschmidt, process is an aluminothermic method for the production of molten iron or steel. The principal feature of the reaction is the exothermic reaction of aluminum and iron oxide in finely divided form to produce iron, aluminum oxide, and considerable heat. The amount of energy generated by the reaction depends upon the formulation, but it is sufficient to melt the iron and to separate it from the alumina slag.



The process is useful for the production of iron and iron alloys entirely by chemical means. No auxiliary heat source is necessary as in smelter-produced iron, but the iron so produced is more expensive than foundry iron. However, it has the advantage of being capable of use anywhere in almost any quantity required. Since alloying elements can be incorporated in the formulations, a wide variety of irons and steels may be made. Because of the flexibility of process and formulation, there is a considerable range of temperature available. The reaction may be held to just above the melting point of the metal produced, or it can be made sufficiently exothermic so as to exceed a peak temperature of 4,000°F. This property of extreme temperature com-

bined with the production of molten metal has led to the nonproductive use of thermit materials in incendiary weapons (see *Incendiaries*).

The process is capable of so many modifications that no general description can be made. Typically, the thermit mixture is charged into a special crucible, and the reaction is started by the use of an ignition powder which furnishes sufficient local heat to initiate the thermit reaction. The chemical reaction proceeds rapidly and is finished in a few seconds to a few minutes. The molten metal produced separates from the alumina slag and may then be tapped into a ladle or directly into a mold. Recently a combined self-tapping crucible and mold has been introduced for welding small cross sections (1).

Uses of the metal produced by the aluminothermic process range from rail welding, repair of heavy machinery castings and forgings, oil drill stems, and large pump housings to the welding of the stern frames of ships. The *Welding Handbook* (2) devotes a chapter to the techniques of many of the common welds utilizing the thermit process, including the preparation of the section to be welded, preheating methods, and the welding process itself. Other welding procedures are available from the producers of aluminothermic materials.

Variations of the aluminothermic technique are used for the producing of special alloys and very pure metals such as ferrotitanium, nickel-titanium, and chromium.

### Bibliography

- (1) Thermit Data Sheet, "Thermit Welding of Reinforcing Bars," Metal & Thermit Corporation, N.Y., August, 1953.
- (2) *Welding Handbook*, 3rd ed., American Welding Society, N.Y., 1950, p. 449.

C. K. BANKS

## THERMOCHEMISTRY

Thermochemistry is a branch of physical chemistry which deals with the heat effects accompanying physicochemical processes. See also *Calorimetry*; *Thermodynamics*. A process is called exothermic if heat is produced by the reaction; or endothermic if heat is absorbed. When heat is neither produced nor absorbed in the reaction, the process is described as thermoneutral. Some physicochemical processes involve changes of forms of energy other than heat. These are described as exoenergetic or endoenergetic depending on whether energy is produced or absorbed in the reaction. An exoenergetic process need not be exothermic; for example, one can construct an electric element that produces electrical energy and at the same time absorbs heat. Here the process is exoenergetic but also endothermic.

Consider a reaction that involves no changes in any form of external energy except heat ( $Q$ ). If no work is done (or taken up) by the reaction, the process must be isochoric, that is, it takes place at constant volume. In such a process the heat is produced on account of the change in the internal energy of the system:

$$\Delta Q = -\Delta E \quad (1)$$

Equation (1) is a special form of the first law of thermodynamics (conservation of energy). Its application allows one to determine experimentally (that is, by calorimetric methods) the changes in the energy of the system when it is transferred from

some initial state *A* to a new state *B*. Since the concept of the absolute value of energy of any system is meaningless, differences in energy are always dealt with. Hence, it may be assumed arbitrarily that the energy of some system (or systems) is zero and thus a value can be ascribed for the energy of any other system (or systems) in relation to this standard. This arbitrary assignment of zero energy level to some systems is restricted to the set of independent systems. For example, it might be assumed that the energy contents of gaseous hydrogen and gaseous oxygen both at normal temperature and pressure are zero. In respect to this standard, the energy content of liquid water is fixed and cannot be arbitrarily chosen, for example, as zero. One might choose, however, the energy content of liquid water and gaseous hydrogen as zero, but then the energy content of gaseous oxygen would be fixed and could not assume any arbitrary value.

It is customary to consider the energy of separated atoms at 0°K. as representing the relative zero level for energy, and thus the energy of any other system is measured by the negative amount of heat produced when the respective atoms are combined into the system in question; for example, the energy of a crystal is equal to the negative amount of heat liberated in the process of formation of the crystal lattice from the separated atoms. The amount of heat absorbed in the reverse process is known as heat of atomization.

Many practical problems deal with processes that take place not at a constant volume but at a constant pressure. In such processes the heat produced in the reaction is given by Equation (2):

$$\Delta Q = -E - p \Delta V \quad (2)$$

where  $\Delta V$  denotes the change in the volume of the system resulting from the reaction. Equation (2) can be rewritten by introducing a thermodynamic function known as the *enthalpy* or the *heat content*, denoted usually by *H* and defined by equation (3):

$$H = E + pV \quad (3)$$

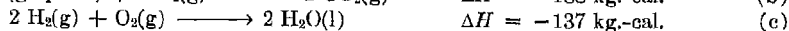
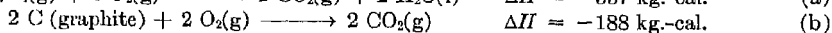
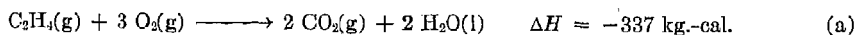
From this definition it follows that in an isobaric (constant-pressure) process  $\Delta H = \Delta E + p \Delta V$  and in any case:

$$\Delta Q = -\Delta H \quad (4)$$

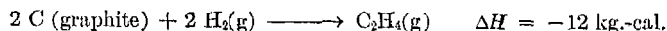
Equation (4) forms the basis of most thermochemical calculations.

**Hess' Law.** Hess showed in 1840 that the heat change in any reaction is independent of the manner in which the reaction is made to proceed. This statement is a consequence of the law of conservation of energy. Its exact formulation should include either of the two conditions: (1) all the processes considered should be isobaric, (2) all the processes considered should be isochoric. If either of these conditions is not stipulated, one can easily construct a cyclic process which consumes heat and produces work or vice versa.

Hess' law has an important application in thermochemistry. There are many reactions that cannot be performed directly in the laboratory and for which the amount of heat produced in the process is sought. For example, assume that for the determination of the heat of formation of ethylene from carbon in the form of graphite and gaseous hydrogen the following set of data are available:



These equations are examples of thermochemical equations, in which the ordinary chemical equation denotes the stoichiometrical quantities of the substances involved and their states of aggregation are denoted by (s), (l), (g), etc. Equations such as these may be treated algebraically and if (b) and (c) are added and (a) is subtracted:

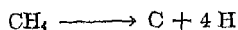


which shows that, when 24 g. of graphite reacts with 4 g. of hydrogen gas to form 28 g. of gaseous ethylene, 12 kg.-cal. is released. Thus the heat change for a reaction is obtained where a direct experimental determination would have been impracticable. Such a computation leads to reliable results if the number of reactions that have to be considered is relatively small. When a large number of reactions has to be considered, the accuracy of the computation will be poor since the errors involved in each individual step are added together.

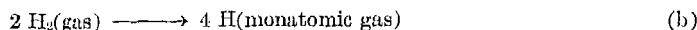
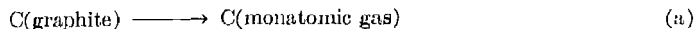
In the above example only a difference in heat content is dealt with. In fact, the concept of the absolute value of the heat content of any element or compound, like the concept of the absolute value of energy, is meaningless. To obtain numerical values for the heat content, a reference state for each element is adopted and it is assumed that its heat content in this state is zero. If the reference states are chosen, values can be assigned to the heat content of any compound. The standard for the heat content is different from the generally accepted standard for zero level of energy. For the sake of convenience, in thermochemistry the heat content of the form of the element which is stable at room temperature and 1 atm. pressure is taken as the reference zero. The heat of formation of a compound is then understood to mean the amount of heat absorbed in the formation of one mole of the compound from its constituent elements in their standard states. It is now customary to refer the results of all thermochemical investigations to 25°C., although many earlier data are given for 18°C.

**Heats of Atomization, Formation, and Combustion.** The heat of atomization has been defined earlier as the amount of heat required to dissociate one mole of a compound into its component atoms, each atom being in its ground state and the process being carried out at absolute zero. On the other hand, the heat of formation of the compound is defined as the amount of heat absorbed in an isobaric and isothermic reaction in which the compound in question is formed from its elements, each of them being in its standard state and the process being carried out at 25°C. and under a pressure of 1 atm.

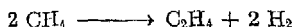
The heat of atomization provides a value for the energy content of a compound, while the heat of formation gives its heat content. The following discussion shows why different standards have been chosen for the energy content and for the heat content. To understand the mechanism of formation of a compound, the nature of the forces that bind the separate atoms into a molecule, the details of molecular structure, etc., the heat of atomization must be known. The magnitude of the heat of atomization characterizes the molecule and describes its absolute thermodynamical stability. Furthermore, the heat of atomization can be calculated, at least in principle, from the fundamental laws of quantum mechanics. Thus the importance of the heat of atomization in theoretical chemistry is obvious. Unfortunately, the heat of atomization of the majority of compounds cannot be determined directly. For example, to calculate the heat of atomization of methane the dissociation process:



has to be investigated but the direct study of this process is impractical. However, the heat of atomization of methane can be computed by using Hess' law. Consider the following reactions:



Reaction (a) involves the heat of sublimation of carbon, reaction (b) the heat of dissociation of hydrogen molecules, and reaction (c) the heat of formation of  $\text{CH}_4(\text{g})$  from elements in standard states. The heat of atomization of methane is computed, therefore, by subtracting the heat of formation of methane from the sum of the heat of sublimation of graphite and twice the heat of dissociation of a hydrogen molecule. The heat of formation of methane from the elements in their standard states is determined with a high degree of accuracy, as is the dissociation energy of the hydrogen molecule; the heat of sublimation of graphite is not known with certainty. Consequently, the value for the heat of atomization of methane is less certain than the value for its heat of formation. The same situation is encountered in many other examples. The heats of dissociation of  $\text{N}_2$ ,  $\text{S}_2$ ,  $\text{F}_2$ , etc. are not known with certainty. Thus we are unable to ascribe final values to the heats of atomization of compounds containing carbon, nitrogen, sulfur, fluorine, and some other elements. On the other hand, heats of many reactions can be computed from heats of formation. For example, the exothermicity of the gaseous reaction:



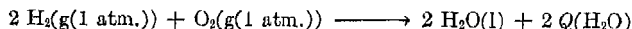
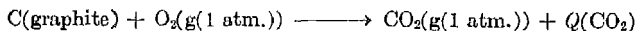
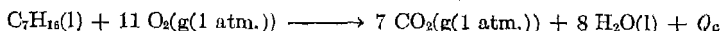
is computed as follows:

$$\Delta Q = \Delta H_f(\text{C}_2\text{H}_6) + 2 \Delta H_f(\text{H}_2) - 2 \Delta H_f(\text{CH}_4)$$

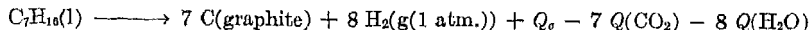
These examples make clear why it is useful to have both standards, one for theoretical work, the other for many calculations that do not penetrate as deeply into problems of molecular structure.

One of the most useful methods of determining the heat of formation of organic compounds which contain only carbon, hydrogen, and oxygen is that which makes use of the observed heats of combustion of the compound and the known heats of formation of carbon dioxide and water. The *heat of combustion* may be determined accurately in many cases because combustion is one of the rare organic reactions that proceed to completion smoothly and quickly and without side reactions. The latter condition is important in all experimental thermochemical investigations.

Once the heat of combustion,  $Q_c$ , has been determined, the heat of formation of the organic compound may be obtained quite simply as follows: Assume, for example, that the heat changes of the following reactions are known:



From these equations:



and therefore  $\Delta H_f$  for the compound  $\text{C}_7\text{H}_{16}$  is given by:

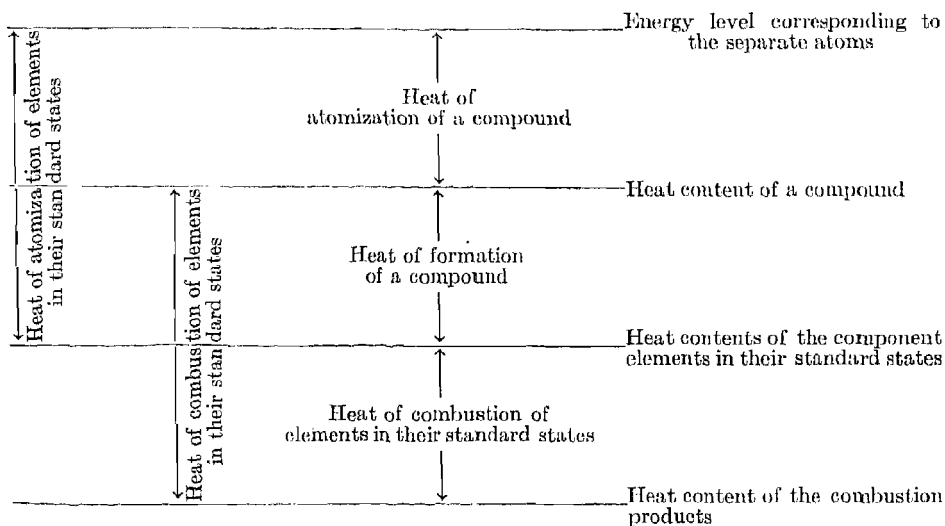
$$\Delta H_f = Q_c - 7 Q(\text{CO}_2) - 8 Q(\text{H}_2\text{O})$$



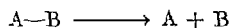
For compounds containing elements other than carbon, hydrogen, and oxygen, the evaluation of the heat of formation from the heat of combustion is complicated by the necessity of determining the final state, both chemical and physical, of these elements. For compounds containing sulfur, for instance, it is often assumed that the sulfur is eventually oxidized to sulfuric acid, although in some cases the formation of sulfur dioxide has been observed. Again, when nitrogen is present, its final chemical state is usually as nitrogen gas, but in some cases the presence of nitric oxide has been reported.

A schematic relation between heats of formation, heats of combustion, and heat of atomization is given in Scheme 1.

SCHEME 1



**Heats of Reaction Involving Radicals and Atoms.** To calculate the heat of a reaction involving radicals and atoms it is necessary to know the heat of formation of these species. These data can be obtained from the values of bond dissociation energies, which in turn can be determined by various experimental techniques. By bond dissociation energy is understood the energy required to rupture the bond in question, that is, the heat of the dissociation reaction:



where A and B denote free radicals or atoms.

There is a simple thermochemical relation between the bond dissociation energy and the heat of formation of radicals. Taking the above-discussed process as an example:

$$D(A-B) = \Delta H_f(A) + \Delta H_f(B) - \Delta H_f(AB)$$

In this equation  $D(A-B)$  denotes the A—B bond dissociation energy, and  $\Delta H_f(A)$ , ... have the usual meaning of heats of formation of species A, ... from the elements in their standard states. This equation permits the computation of the heat of for-

mation of the free radical or atom A, providing that the heat of formation of the compound AB, the bond dissociation energy, and the heat of formation of the other radical (or atom) B are determined independently.  $D(A-B)$  can be determined by specially designed experiments, and the determination of  $\Delta H_f(AB)$  is straightforward. Hence, the only difficulty arises in the necessity of determining of  $\Delta H_f(B)$ . This difficulty can be resolved by determining the dissociation energy of symmetrical molecules, such as  $H-H$ ,  $Br-Br$ , and  $NH_2-NH_2$ . For such molecules, the thermochemical equation takes the following form:

$$D(A-A) = 2 \Delta H_f(A) - \Delta H_f(A_2)$$

and therefore

$$\Delta H_f(A) = \frac{1}{2} \{ D(A-A) + \Delta H_f(A_2) \}$$

The heats of formation of some atoms or radicals having been determined in this way, the previous equation can be used for determining the unknown heats of formation of other radicals.

**Specific Heat and Heat Capacity.** The *heat capacity* of a substance is the amount of heat required to heat a given weight of it through one degree centigrade. Heat capacity may be calculated per mole of substance, or per gram, in which case the term *specific heat* is also applicable. The measurement may be made at constant pressure or at constant volume, giving:

$$C_p = \left( \frac{\partial H}{\partial T} \right)_p \quad \text{and} \quad C_v = \left( \frac{\partial H}{\partial T} \right)_v$$

According to the law of equipartition of energy, the average kinetic energy associated with each degree of freedom is  $RT/2$  per mole, and thus the heat capacity associated with each degree of freedom is  $R/2$ . For diatomic and linear polyatomic molecules there are 3 degrees of translational freedom, 2 degrees of rotational freedom, and  $3n - 5$  degrees of vibrational freedom, where  $n$  is the number of atoms in the molecule. For other polyatomic molecules there are 3 degrees of translational freedom, 3 degrees of rotational freedom, and  $3n - 6$  degrees of vibrational freedom. Simple kinetic theory does not consider the vibrations of a molecule but treats it as a rigid body. If we ignore the degrees of vibrational freedom, we find from the simple theory that the heat capacities of gases at constant pressure are  $(5R/2) + R = 6.96$  cal./mole(°C.) for diatomic and linear molecules, and  $4R = 7.95$  cal./mole(°C.) for polyatomic molecules. Since the vibrations have been neglected, we would expect these values to be low, and this is found to be the case. The values actually represent lower limits to the heat capacities.

**Recalculation of the Heat of Reaction for Another Temperature.** The heat of reaction for a particular process is usually given at some specific temperature, but it is often necessary to know the heat of this reaction at some other temperature. This information can be easily obtained if the heat capacities of the reactants and products are known.

By definition:

$$\Delta C_p = \left( \frac{\partial \Delta H}{\partial T} \right)_p$$

Consider the reaction:



Then:

$$\Delta H = qH(C) + rH(D) - nH(A) - mH(B)$$

where the  $H$ 's are the molar heat contents for the compounds A, B, C, and D. Similarly, the heat capacity change is:

$$\Delta C_p = qC_p(C) + rC_p(D) - nC_p(A) - mC_p(B)$$

The dependence of the heat capacity of a substance on temperature may usually be represented by a power series of the form:

$$C_p = a + bT + cT^2 + dT^3 + \dots$$

and thus:

$$\Delta C_p = \alpha + \beta T + \gamma T^2 + \delta T^3 + \dots$$

(the terms  $\alpha$ ,  $\beta$ , etc., are obtained approximately from the  $a$ ,  $b$ , terms for the various substances according to the equation for  $\Delta C_p$ ). Therefore:

$$\left( \frac{\partial \Delta H}{\partial T} \right)_p = \alpha + \beta T + \gamma T^2 + \dots \quad (4a)$$

On integration:

$$\Delta H = \alpha T + \frac{\beta T^2}{2} + \frac{\gamma T^3}{3} + \dots - \Delta H_0 \quad (5)$$

where  $\Delta H_0$  is the change in heat content, that is, heat of reaction, at the temperature of absolute zero. Integration between limits of temperature  $T_1$  and  $T_2$  leads to:

$$\Delta H_{T_2} - \Delta H_{T_1} = \alpha \Delta T + \beta \frac{(\Delta T)^2}{2} + \gamma \frac{(\Delta T)^3}{3} + \dots \quad (6)$$

where  $\Delta T = T_2 - T_1$ . Equation (6) enables us to compute the heat of reaction  $\Delta H_{T_2}$  if we determine the heat of reaction at one temperature,  $T_1$ , and know the temperature dependence of the specific heats of the reactants and products. For instance, for the reaction:



The molal heat capacities are:

$$\begin{aligned} \text{H}_2 &= 6.54 + 0.0007T \\ \text{O}_2 &= 6.69 + 0.0007T \\ \text{H}_2\text{O} &= 8.81 - 0.0019T + 0.00000222T^2 \end{aligned}$$

Hence:

$$\begin{aligned} \Delta C_p &= 2(8.81) - 6.69 - 2(6.54) - 2(0.0019T) - 0.0007T - 2(0.0007T) + \\ &\quad 2(0.00000222T^2) \\ &= -2.16 - 0.0059T - 0.000004444T^2 \end{aligned}$$

Assume that it is required to calculate the heat of reaction at 1100°C. (1373°K). By applying equation (6):

$$\begin{aligned}\Delta H_{1373} &= \Delta H_{373} - \int_{373}^{1373} C_p dT \\ &= -116,115 - (-2.16)1,000 - \frac{0.0058 \times 1,000 \times 1,000}{2} + \\ &\quad \frac{0.00000444 \times 1,000^3}{3} \\ &= -116,115 - 2,160 - 2,900 + 1,480 \\ &= -119,695 \text{ cal.}\end{aligned}$$

**Thermal Effects Accompanying Physical Changes of State.** The heat effects accompanying the transition from one physical state to another, such as the heat of fusion, heat of vaporization, and heats of transition, are important data which are often used in calculating heats of reaction and entropies of pure substances.

*Latent Heats of Vaporization.* The molal latent heat of vaporization is defined as the quantity of heat absorbed by one gram-mole of the substance when transferred from liquid to vapor at a constant temperature. The quantity may be measured, for instance, by an equilibrium method in which the amount of electrical energy supplied to the liquid is balanced by the heat energy lost through vaporization.

A relationship known, as the Clausius-Clapeyron equation, between the latent heat of vaporization and the vapor pressure also may be used in the determination of the heat of vaporization. This relationship may be expressed as:

$$\frac{d \ln p}{dT} = - \frac{\Delta H}{RT^2}$$

where  $p$  is the saturated vapor pressure of the liquid at temperature  $T$ . In deriving this equation, we assume that the vapor obeys the ideal gas laws and that the specific volume of the liquid is small compared with that of the vapor. Integration of the above equation gives:

$$\ln \frac{p_1}{p_2} = \frac{\Delta H}{R} \left( \frac{T_2 - T_1}{T_2 T_1} \right)$$

Hence, if the vapor pressure of the liquid is known at two temperatures,  $\Delta H$  may be calculated. For example, Kahlbaum and Wirkner found that at 293°K. the vapor pressure of benzene is 75.0 mm. and at 303°K. it is 118.0 mm. and from these data they calculated  $\Delta H = 7,990$  cal.

The Clausius-Clapeyron equation may be put in the form:

$$\frac{-\Delta H}{T} = \frac{R d \ln P_r}{d \ln T_r}$$

where  $P_r$  is the "reduced" pressure  $P/P_c$ , and  $T_r$  is the reduced temperature  $T/T_c$ ,  $P_c$  and  $T_c$  are the critical pressure and temperature, respectively. From the theory of corresponding states, the  $d \ln P_r / d \ln T_r$  term should have the same value for all substances in corresponding states. Guldberg, in 1890, showed that for a large number of substances the boiling point (in degrees absolute) is approximately  $\frac{2}{3}$  of the critical temperature. Hence, two liquids at the boiling point may be considered to be in corresponding states. Thus, the molal heats of vaporization divided by the absolute boil-

ing points, that is, the entropy of vaporization of compounds, should be approximately a constant. This conclusion is known as *Trouton's rule*, and it is found that the entropy of vaporization for a number of nonassociated liquids has a value of about 20–23, known as the Trouton constant. If, however, the relationship is examined for liquids with widely different boiling points, marked differences are observed. Trouton's rule also fails for liquids that are associated such as water, acetic acid, and ethyl alcohol, and, in general, for liquids containing hydroxyl groups.

Hildebrand proposed a modification to the rule for nonpolar liquids. Instead of comparing the entropies of vaporization at the boiling point, he suggested that they be compared at temperatures where the vapor concentrations are the same. Polar liquids however, again deviate from the rule.

Although these rules are useful in interpreting the observed value of an entropy of vaporization and in predicting the degree of ordering or association in the liquid state, they are often insufficiently reliable for the calculation of the exact values of heat of vaporization.

*Heats of Fusion.* The molal heat of fusion of a solid compound is defined as the amount of heat required to convert 1 gram-mole of the compound from the solid state to the liquid state at the melting point. We may regard the process of melting as one in which the forces that hold the solid crystal together are being overcome with a consequent increase in the degree of freedom of the molecules in the liquid state over that in the solid state. The heat of fusion may be regarded, therefore, as a measure of the magnitude of the forces operating in the crystal, and the entropy of fusion,  $S_f$ , as a measure of the increased freedom of the molecules. For solids that undergo similar internal processes in melting, it would be expected that some constancy of the entropy of fusion might be observed. In practice, certain generalizations may be made. It is found that for most elements:  $S_f = 2\text{--}3$  e.u.; for most inorganic compounds:  $S_f = 5\text{--}7$  e.u.; for most organic compounds:  $S_f = 9\text{--}11$  e.u. There are, of course, many exceptions to the above rules. For instance, for hydrogen chloride and bromide, the entropies of fusion are about 3.0 e.u. It is known from other sources that the molecules of hydrogen chloride and bromide are rotating about their centers of gravity in the solid states. Hence, since this degree of freedom would normally only appear on melting, it would be expected that entropy of fusion would be lower than the normal value. Provided that the limitations of the above generalization are kept in mind, the entropy of fusion may be used to provide useful information about the internal state of a crystal.

*Heats of Transition.* On heating, many substances exhibit regions of heat absorption with no corresponding rise in temperature. Such phenomena are thought to be due to the change in the crystal structure of the substance or the appearance of an extra degree of freedom, for example, rotation, as was noted above in the crystals hydrogen chloride and bromide. To demonstrate the existence of such a transition one has to rely often on experimental observation of the very small heat effect accompanying it. In the fusion of hydrogen chloride and bromide we might expect the existence of a transition due to the freezing of rotation of molecules. The entropy of this transition added to the observed entropy of fusion should then give a value in the normal range of 5–7 e.u. Indeed such a transition has been observed, and the entropy change taking place during this transition is 2.89 e.u. This value added to the entropy of fusion leads to 5.89 e.u., which is the normal magnitude for entropy of fusion of inorganic compounds.

**Heats of Reaction from Equilibrium Constants.** Consider the reaction:



The standard free-energy change for the reaction may be expressed as:

$$-\Delta G^0 = RT' \ln K \quad (7)$$

for the systems in equilibrium. This expression is of the greatest use in determining the feasibility of a particular chemical reaction as an industrial process.  $\Delta G^0$  represents the free-energy change corresponding to the production of the indicated number of the products C, D, etc., in their standard states from the indicated number of moles of reactants A, B, etc., in their standard states. These standard states are states of unit activity (or fugacity). It will be seen from equation (7) that, if the standard free-energy change,  $\Delta G^0$ , is positive, the conversions obtained at equilibrium for a particular reaction are likely to be less profitable than for a reaction where the free-energy change is negative. (Conversely, if  $-\Delta G^0$  is considered, this will be positive for a reaction which proceeds from the left to the right of the equation as written, and negative if it proceeds from the right to the left.)

We can now consider the change in equilibrium constant with temperature. For reversible reactions:

$$\left(\frac{\partial G}{\partial T}\right)_p = \frac{\Delta G - \Delta H}{T} \quad (8)$$

This is known as the Gibbs-Helmholtz equation. It may be rewritten in the form:

$$\frac{d}{dT} \left( \frac{\Delta G^0}{T} \right) = \frac{-\Delta H}{T^2}$$

By substituting equation (7) in this expression we obtain:

$$\frac{d \ln K}{dT} = \frac{-\Delta H}{RT^2} \quad (9)$$

Therefore, the direction in which the equilibrium constant changes with temperature depends only on the change in heat content. If the reaction is endothermic, that is, if  $\Delta H$  is positive, the equilibrium constant increases with increasing temperature, whereas, if  $\Delta H$  is negative, the equilibrium constant decreases with increasing temperature. Hence the conversion in an endothermic reaction increases with increasing temperature, whereas in an exothermic reaction the contrary is true.

To use the Gibbs-Helmholtz equation we may assume, if the temperature range is small, that  $\Delta H$  is a constant and integrate the equation directly to obtain:

$$\log \frac{K_2}{K_1} = \frac{-\Delta H}{2.303R} \frac{T_2 - T_1}{T_2 T_1} \quad (10)$$

In the general case  $\Delta H$  may be expressed as a function of temperature by means of an expression of the type of equation (5). Substituting this in equation (9):

$$R \ln K = \frac{-\Delta H^0}{T} + \alpha \ln T + \frac{\beta}{2} T + \frac{\partial T^2}{3} + \dots + I \quad (11)$$

where  $\alpha$ ,  $\beta$ , etc., have the significance of equation (5) and  $I$  is a constant of integration.

In order to apply this equation to determine  $\Delta H_0$ , it is necessary to know the value of the equilibrium constant at two temperatures, the change in heat capacities, and the heat of reaction at a definite temperature. If the entropy change can also be calculated,  $\Delta G$  can then be found from  $\Delta G = \Delta H - T\Delta S$ .

We may evaluate the heat of reaction of a particular process if we know the variation of the equilibrium constant with temperature and the heat capacities of reactants and products. Equation (11) may be written

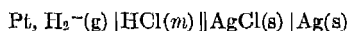
$$R \ln K - \alpha \ln T - \frac{\beta}{2} T - \frac{\gamma}{3} T^2 = \frac{-\Delta H_0}{T} + I \quad (12)$$

The left side of this equation is a determinable quantity, and this quantity may be plotted as a function of  $1/T$ . The slope of the line so obtained will give  $-\Delta H_0$  directly. Hence  $\Delta H$  may be calculated at any temperature  $T$  from the relationship:

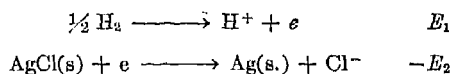
$$\Delta H = -\Delta H_0 + \alpha T + \frac{\beta T^2}{2} + \frac{\gamma T^3}{3}$$

It is often possible to obtain accurate values for the heat of reaction by this method when the values obtained calorimetrically are unreliable.

**Evaluation of  $\Delta G^0$  and Heats of Reaction from E.M.F. Measurements** (see also *Electrochemistry; Oxidation-reduction*). This method is not applicable to all reactions since it is not always possible to construct a cell that will produce the desired change. If, however, a cell will bring about the desired change, we may calculate the standard free energy of the reaction from the standard e.m.f. of the cell. For example, in the cell:



the change taking place in the cell may be represented as:



Hence the total e.m.f. is:

$$E = E_1 - E_2 = E_1^0 - E_2^0 - \frac{RT}{F} \ln \frac{\alpha(\text{HCl})}{f(\text{H}_2)^{1/2}}$$

$\alpha(\text{HCl}) = \alpha(\text{H}^+) \cdot \alpha(\text{Cl}^-) = (\gamma m)^2$ , where  $m$  is the molality of  $\text{HCl}$  and  $\gamma$  is the activity coefficient, and  $f(\text{H}_2)$  is the fugacity of hydrogen, assumed here to be unity, and  $E_1^0$  is the standard hydrogen electrode potential taken by convention to be zero. Therefore:

$$E_2^0 \approx -E - RT \ln (\gamma m)^2 \text{HCl}$$

The observed cell e.m.f. at  $25^\circ\text{C}$ . is 0.4586 volt. If the molality of  $\text{HCl}$  is 0.112 and the corresponding activity coefficient is 0.903:

$$E_2^0 = -0.2220 \text{ volt}$$

Thus the standard e.m.f. of the cell is  $E_1^0 - (-E_2^0) = -0.2220 \text{ volt}$ .

$$-\Delta G_{298.1}^0 = NFE = 5,120 \text{ cal.}$$

If we know the variation of the standard e.m.f. of the cell over a particular range of temperature, we may calculate the heat of reaction at a particular temperature within the range by means of the Gibbs-Helmholtz equation:

$$\left[ \frac{\partial(\Delta G^0)}{\partial T} \right]_p = \frac{\Delta G^0 - \Delta H}{T} \quad (13)$$

Substituting:

$$\begin{aligned} -\Delta G^0 &= NFE^0 \\ -NF \frac{\partial E^0}{\partial T} &= - \frac{NFE^0 - \Delta H}{T} \\ \Delta H &= T NF \left( \frac{\partial E^0}{\partial T} \right)_p - NFE^0 \end{aligned}$$

from which we may calculate  $\Delta H$ .

### Bibliography

- (1) Bichowsky, F. R., and Rossini, F. D., *The Thermochemistry of the Chemical Substances*, Reinhold N.Y., 1936.
- (2) Marshall, A. L., "Thermochemistry," in *Treatise on Physical Chemistry*, H. S. Taylor, ed., Vol. I, Van Nostrand, N.Y., 1924.
- (3) Rossini, F. D., *Chemical Thermodynamics*, Wiley, N.Y., 1950.
- (4) Wenner, R., *Thermochemical Calculations*, McGraw-Hill, N.Y., 1941.

MICHAEL SZWARC AND J. J. THROSSEL



